VOLUME 12
NUMBER 11
NOVEMBER, 1959

ORAL SURGERY
ORAL MEDICINE
and ORAL PATHOLOGY

OPERATIVE ORAL SURGERY

GIANT-CELL REPARATIVE GRANULOMA AND RELATED CONDITIONS AFFECTING THE JAWBONES*

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DESPITE major recent advances in our knowledge of pathology of bone tumors in general, confusion still pervades much of the literature on "giant-cell tumor" of the jaws. Oral surgeons and pathologists alike are frequently at a loss to predict the potential clinical behavior of a benign giant-cell-bearing lesion in the jaw.

To ascertain what type of benign giant-cell-containing lesions had been observed and to determine what clinical properties the various lesions possessed, a study was made of all cases of pertinent tumors of the jaw encountered at the Mayo Clinic from 1905 through 1956. Of the 426 cases perused, we included only those in which the patients had tumors with osseous involvement evidenced either by roentgenographic signs of cortical or medullary osteolytic reaction or by surgical proof that the tumor had eroded bone or that bone had to be removed in order to expose the tumor. It has been adequately established that giant-cell epulides of the gingival soft tissues are clinically tumefactions that respond readily to surgical removal.[1, 2] Therefore, such tumors without osseous involvement were excluded.

A group of 107 tumors that involved bone remained for further study. A number of these were discarded because of insufficient material to establish an accurate histopathologic diagnosis. Five examples of fibrous dysplasia, two of myxofibromas, and one each of aneurysmal bone cyst, cherubism, neurofibroma, and hemangioma, all of which contained giant cells, were encountered

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*Abridgment of thesis submitted by Dr. Austin to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Dentistry.

and deleted from the definitive studies. Frankly malignant tumors, such as osteogenic sarcomas containing benign or malignant multinucleated cells, also were excluded.

There remained sixty-four lesions which conformed to the histologic description of giant-cell reparative granuloma given by Jaffe.[3] Only two additional tumors possessed the criteria necessary for the diagnosis of genuine giant-cell tumor of bone.[4] One of these latter tumors occurred in a 12-year-old boy who had had a painless swelling of the left hard palate for two and one-half weeks (Fig. 1). Roentgenograms showed evidence of an oval radiolucent defect. Excision of the lesion by curettage has resulted in eight and two-thirds years of freedom from symptoms. The second giant-cell tumor occurred in a

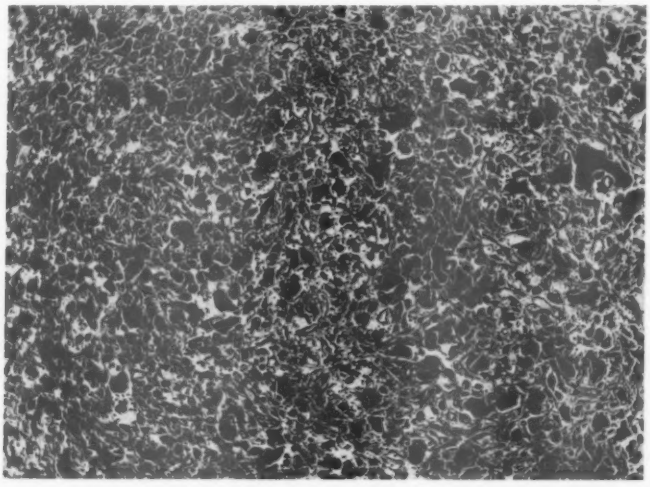

Fig. 1.—Genuine giant-cell tumor of the jaw. Note absence of intercellular substance. (Hematoxylin and eosin stain. Magnification, ×120.)

43-year-old woman who had had pain and swelling referable to her right antrum for two months. This tumor bulged into and produced radiopacity of the antrum. It recurred ten months after the initial treatment by curettage, electrocoagulation, and radon implantation and again seventeen months after curettage and electrocoagulation for the first recurrence. Curettage, diathermy, and roentgen therapy for the second recurrence have finally produced an eight-year remission.

GIANT-CELL REPARATIVE GRANULOMA

For purposes of this study, the upper jaw was defined as the bony alveolus, the hard palate, and the maxillary portion of the walls of the maxillary sinuses. In this series there were three tumors which appeared predominantly within the antrum, but since they obviously arose in the maxilla they were included among the tumors of the upper jaw.

The giant-cell reparative granulomas that involved bone were divided into two types—central and peripheral. Central tumors were those in which a bony covering could be demonstrated either by roentgenographic examination or at the time of surgical exposure. Peripheral tumors occurred as alveolar epulides associated with varying degrees of underlying osseous resorption. In the mandible this resorption varied from a shallow alveolar saucerization to almost complete loss of the mandibular substance in the affected region. Whether the peripheral tumors arose in the soft tissue and secondarily involved the bone or vice versa could not be proved. In some instances alveolar destruction was so advanced that the so-called peripheral tumors actually may have had a central origin. Assuming the three predominantly antral tumors to be central in origin, there were thirty peripheral and thirty-four central tumors in the entire group of giant-cell reparative granulomas.

Incidence.—The files from which these sixty-four lesions were gleaned listed 968 benign tumors of the jaw, an incidence of 6.6 per cent.

TABLE I. AGE OF PATIENTS AT TIME OF TREATMENT

AGE, YEARS	NUMBER OF CASES	
	CENTRAL TUMORS	PERIPHERAL TUMORS
0-9	6	2
10-19	10	4
20-29	5	4
30-39	6	5
40-49	1	7
50-59	5	1
60-69	1	6
70-79	—	1
Total	34	30

Age.—At the time of treatment at the clinic the patients ranged in age from 4 to 70 years (Table I). The average age for patients with central tumors was 26.1 years, and for those with peripheral tumors it was 39.1 years. Whereas 61.8 per cent of the central tumors occurred in patients in the first three decades of life, 53.3 per cent of the peripheral tumors occurred in patients who were between the ages of 19 and 50. More than one-third of all the patients were less than 20 years of age.

Sex.—There were thirty-five females and twenty-nine males. This slight preponderance of females was noticed for both central and peripheral tumors, being 58.8 per cent for the former and 53.3 per cent for the latter type.

Location.—As shown in Table II, the lesions involved the maxilla in twenty-nine cases and the mandible in thirty-five. When the maxilla and mandible were each divided into thirds (that is, an anterior portion and two lateral portions), no anatomic site of predilection was observed.

TABLE II. LOCATION OF CENTRAL AND PERIPHERAL TUMORS

	CENTRAL	PERIPHERAL	TOTAL
Maxilla	15	14	29
Mandible	19	16	35
Total	34	30	64

Signs and Symptoms.—Local swelling, the most important clinical feature, had been noted by sixty of the sixty-four patients. Three tumors were found during routine examination, and the complaint of localized tenderness disclosed the remaining tumor. Pain occurred in 25 per cent of the patients with central tumors and in 10 per cent of those who had peripheral tumors. An additional one-fifth of the patients with central and peripheral tumors complained of local tenderness or discomfort. One central tumor produced anesthesia in the region of the lesion.

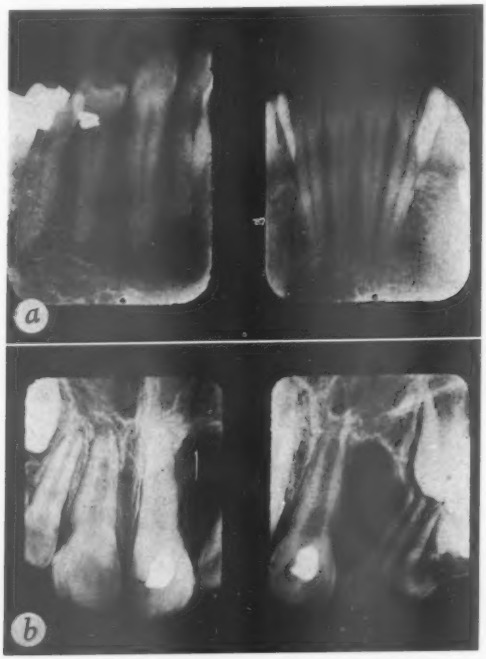

Fig. 2.—*a*, Central giant-cell reparative granuloma in the mandible with absorption of lamina dura and destruction of trabecular architecture. *b*, Giant-cell reparative granuloma in the maxilla with absorption of lamina dura and dental displacement. This was the only tumor in this series which had a radiopaque periphery.

Duration of Signs and Symptoms.—Fairly accurate data regarding the duration of symptoms in the eighteen patients who had not had prior therapy were available. Six of the eighteen patients had central tumors, two of which were found during routine examination. The average duration of symptoms for the other four patients with central tumors was 2.5 months. Ten of the twelve patients with untreated peripheral tumors had had signs and symptoms for an average of 8.1 months; two tumors had been essentially asymptomatic and were found during routine examination.

Roentgenographic Manifestation.—Periapical dental roentgenograms, lateral views of the jaw, and posteroanterior views of the skull were available for

study in twenty-four of the sixty-four cases of giant-cell reparative granulomas. In these twenty-four cases, eleven of the tumors were central and thirteen were peripheral. Ten of the eleven central tumors and six of the thirteen peripheral tumors were in dentulous portions of the alveolar processes. The remaining central tumor occurred at the angle of the mandible, and the other seven peripheral tumors were present in edentulous jaws.

Variable portions of the lamina dura, the cortical bone adjacent to the dental roots, were absorbed in nine patients who had central tumors and in three who had peripheral tumors (Fig. 2, *a*). Six of the central tumors and two of the peripheral tumors caused displacement of the teeth (Fig. 2, *b*). Seven central tumors bulged the cortex in varying degrees, and three others had partially perforated the attenuated, expanded cortex. Only one of the central tumors had a multilocular appearance. Fuzzy densities due to mineralized trabeculae were discernible in the substance of eight of the central and four of the peripheral lesions. In most instances the radiolucent defects produced by both central and peripheral tumors were sharply delineated, and in one instance a sclerotic margin was observed.

Pathologic Aspects.—Practically all of the preserved surgical gross specimens had fibrotic zones, and many of them contained hemorrhagic or calcific foci. The histopathologic features of the sixty-four central and peripheral giant-cell reparative granulomas were studied in detail and compared with the two giant-cell tumors of the jaws and a group of fourteen giant-cell tumors of other bones. Random selection of representative microscopic fields was employed because of the variations observed in different portions of these tumors. An average of four microscopic fields was studied for each feature to be described.

At low magnification (×40) there was no appreciable difference in the number of giant cells in the central and peripheral giant-cell reparative granulomas. The average field of a genuine giant-cell tumor, however, contained four times as many benign multinucleated cells and more nuclei, on the average, than did the reparative granulomas.

Collagen was a prominent component in all of the central and peripheral giant-cell reparative granulomas (Fig. 3, *a*), whereas in the giant-cell tumors of bone large zones without collagen were constantly observed. Osteoid production (Fig. 3, *b*) was observed in half of the central and more than one-third of the peripheral giant-cell reparative granulomas and was much less conspicuous in the giant-cell tumors.

Mitotic figures were less abundant in both central and peripheral reparative granulomas than in the giant-cell tumors. Lymphocytes and erythrocytes were found in practically all tumors studied and thus offered little or no differential diagnostic help.

The basic proliferating cells in all giant-cell reparative granulomas contained an oval or spindle-shaped nucleus and had a prominent nuclear membrane and small nucleolus. Nuclear hyperchromatism, anisocytosis, and irregularities in nuclear shape suggestive of malignant disease were absent. The

elongated shape of the nuclei and the basically fibrogenic or even osteogenic quality of the cells of the reparative granulomas are features that best differentiate this lesion from genuine giant-cell tumors, the cells of which, in unaltered fields, have round or oval nuclei and do not produce recognizable ground substance.

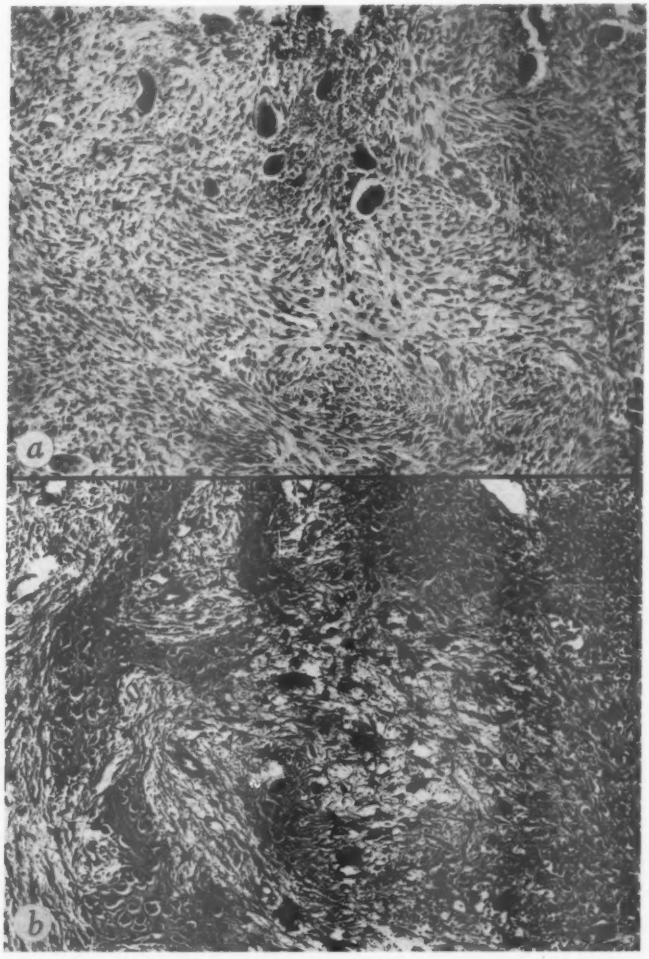

Fig. 3.—*a*, Giant-cell reparative granuloma. Note the fibrogenic quality of the proliferating cells. (Hematoxylin and eosin stain. Magnification, ×100.) *b*, Giant-cell reparative granuloma showing orderly arrangement of osteoid trabeculae. (Hematoxylin and eosin stain. Magnification, ×120.)

Treatment.—Of the sixty-four patients with reparative granulomas, forty-five had had various ineffective forms of treatment, such as extraction of teeth in the involved region, "drainage," "scraping the bone," partial excision

of the tumor, and biopsy. These therapeutic attempts had often been based on erroneous diagnoses. Definitive treatment at the clinic varied widely, since the series encompassed a period of fifty years. Curettage, with or without electrocoagulation, was used in the majority of the cases. Dental extraction was performed when teeth were intimately associated with or actually included in the tumor process. In eight instances adjunctive irradiation therapy was used.

Follow-up information was available in forty-five of the sixty-four cases. The symptom-free interval that had elapsed since treatment ranged from three months to 44.5 years, with an average of 10.7 years for central tumors and 8.3 years for peripheral tumors. Only two recurrences, at intervals of two and three months, respectively, were observed; both developed in central tumors which had been treated by curettage and electrocoagulation. A second similar treatment produced a cure of more than twenty years' duration in each of these two cases.

A sarcoma developed in one of the nine patients who received radiation; the case, that of a 9-year-old boy, has been reported in detail previously.[5] After extraction of a tooth, there developed a tender mass that filled the left antrum and expanded the maxilla. A tumor 5 cm. in diameter was excised, and roentgen and radium treatments were administered. Seven years later an osteogenic sarcoma developed in the same region. Despite wide excision of the sarcoma, recurrence with local extension into the brain produced death within 9 months.

COMMENT

This study corroborates the conclusion that giant-cell reparative granuloma is a distinctive benign tumefaction of the jaws. A detailed study of more than 2,000 primary tumors of bone by one of us[6] supports the idea that this lesion, in its typical form, rarely, if ever, occurs in bones other than those of the jaws. It is histologically distinct from genuine giant-cell tumor of bone in that its proliferating cells are basically fibrogenic and have a marked tendency to undergo metaplasia to a type of cell capable of producing osteoid and bone. Many of the lesions develop more or less parallel osseous trabeculae reminiscent of those seen in a callus (Fig. 3, *b*). There appears to be little or no essential difference in the histology or the basic biologic behavior of giant-cell reparative granulomas of the central and peripheral types.

The histopathology of these reparative granulomas strongly suggests that they are reactive rather than neoplastic. Although several theories have been advanced,[3, 7-9] the cause of these tumors is still unknown. Some have observed that these lesions, especially when recurrent, may develop on the basis of an underlying hyperparathyroidism.[3, 10, 11] Our study suggests that such a relationship rarely exists, since none of the sixty-four pertinent examples studied were related to proved hyperparathyroidism.

The name "granuloma" may be misleading when applied to this tumor of the jaw. The average pathologist considers a granuloma to be a more obviously inflammatory lesion, the most significant feature of which is its component of epithelioid cells which often appear in a palisaded arrangement.

The term "giant-cell reparative granuloma" is gaining increasing acceptance, however, and it seems unwise to suggest a different nomenclature because of this minor point.

The roentgenologic features of giant-cell reparative granuloma, whether central or peripheral, are basically nonspecific. The zone of fairly discretely outlined rarefaction suggests that the lesion is probably benign, but a similar appearance can be produced by other lytic processes in bone.

The differential diagnosis of giant-cell reparative granuloma includes all lesions of the jaw that contain benign multinucleated cells.

Genuine Giant-Cell Tumor.—This tumor of bone is distinctly rare in the jaws. Although Waldron[11] stated that five of twenty-six cases of giant-cell-bearing lesions of the jaws were giant-cell tumors, Jaffe,[3] in his vast experience, encountered only one case. In the current study there were only two giant-cell tumors, as contrasted with sixty-four giant-cell reparative granulomas. The histologic differentiation is based on the fact that the cells of the former tumor do not produce a recognizable intercellular substance, such as collagen or osteoid, in diagnostic fields. Of perhaps less significance is the fact that mitotic figures tend to be more prevalent and giant cells more numerous in the true giant-cell tumors. Giant-cell reparative granulomas affect a somewhat younger age group on the average than do giant-cell tumors, the latter tumors being distinctly unusual in patients less than 20 years of age. A more important clinical difference is that giant-cell tumors recur in at least 50 per cent of cases after conventional methods of therapy and 10 per cent become malignant.

Aneurysmal Bone Cyst.[12]—One example of this variant of giant-cell tumor was encountered in the present study of tumors of the jaw. Like giant-cell reparative granulomas, this lesion tends to be distinctly fibrogenic and also produces osteoid, frequently in abundance. The histologic differentiation is based on the finding of cavernomatous blood-filled spaces in aneurysmal bone cyst (Fig. 4, *a*). These spaces are so prominent that the average lesion is extremely hemorrhagic at the time of surgical intervention. Except for the blood-filled spaces, as already indicated, aneurysmal bone cyst and giant-cell reparative granuloma have many histologic similarities. In addition, both lesions probably are not neoplastic, are of unknown etiology, and are equally responsive to conservative therapy; they also affect about the same age group. A strong kinship undoubtedly exists between these two lesions, both of which probably represent peculiar reactions to osseous injury of unknown type.

Cherubism.—This condition may be confused with giant-cell reparative granuloma, since the lesion contains distinctly fibrogenic tissue and scattered benign giant cells as well as osteoid trabeculae (Fig. 4, *b*). The fibrous tissue tends to have an edematous appearance, histologically, but the main differentiation rests on clinical grounds. Unlike giant-cell reparative granuloma, cherubism is distinctly familial and characteristically affects the jaws bilaterally.

Fibrous Dysplasia.—The dense collagen of fibrous dysplasia contains variable amounts of irregularly disposed osteoid and bony substance (Fig. 4, *c*).

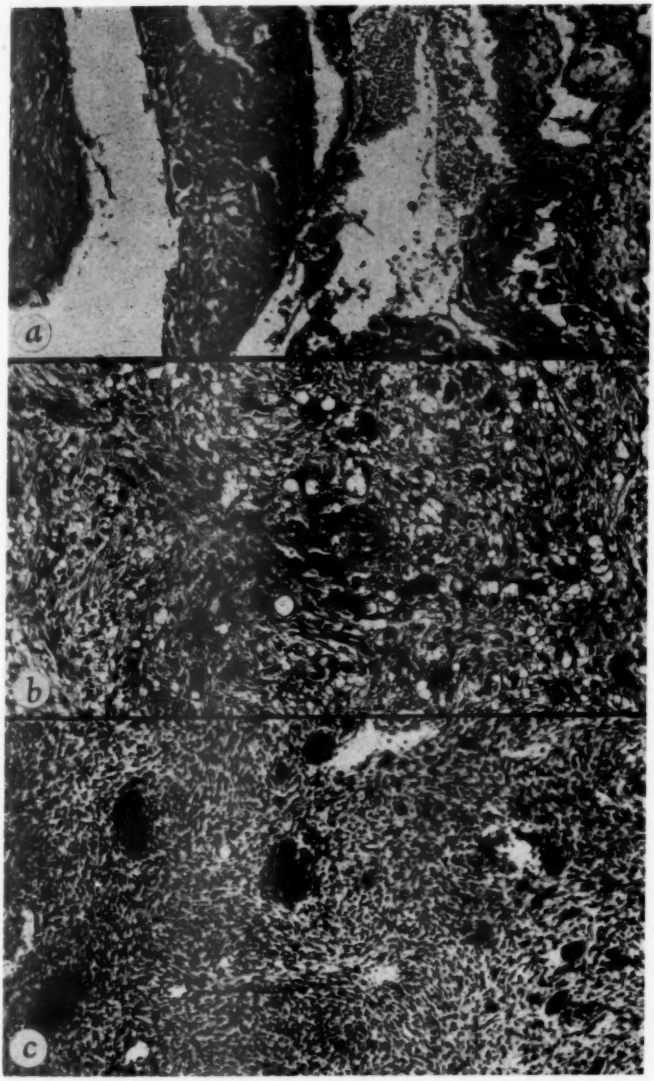

Fig. 4.—*a*, Aneurysmal bone cyst showing partially collapsed blood spaces and fibrous septa containing giant cells. (Hematoxylin and eosin stain. Magnification, ×120.) *b*, Lesion of jaw in cherubism. Note the edematous stroma and giant cells. (Hematoxylin and eosin stain. Magnification, ×120.) *c*, Fibrous dysplasia containing three osseous trabeculae on the left and giant cells associated with extravasated blood. (Hematoxylin and eosin stain. Magnification, ×90.)

Only in rare instances do hemorrhagic or degenerative zones of fibrous dysplasia contain benign multinucleated cells. In such instances adequate sampling of the lesion usually discloses the typical histologic features as described. The trabeculae, when present, lack the orderly, functional appearance of trabeculae seen in giant-cell reparative granuloma.

Soft-Tissue Giant-Cell Epulides.—These tumefactions on the jaws frequently do not involve bones. Histologically, they are much like giant-cell reparative granulomas and are no doubt closely related to them.

Other benign giant-cell variants, such as chondroblastoma,[13] must be considered, but as yet they have not been described in the jawbones.

Occasional malignant tumors of bone, such as osteogenic sarcoma and myeloma, may contain benign multinucleated cells. In some cases these tumors have been mistaken for giant-cell reparative granuloma, with resultant disastrous undertreatment. Recognition of these malignant tumors depends on cytologic evaluation of the proliferating elements.

The present study, like studies of other authors,[3, 8, 11] indicates that conservative surgical management is adequate for giant-cell reparative granulomas. Complete enucleation of the tumor practically always results in cure. In rare instances the region about the lesion will be replaced by a tumor that resembles the original one. This should not be surprising, since the etiology of giant-cell reparative granuloma is unknown and it seems quite reasonable that in some cases such tissue might fill a surgical defect. In fact, one of the tumors in the present series developed in the region from which a cyst had been recently excised.

More aggressive treatment than that indicated herein may be dangerous. Certainly, it is unnecessary to resort to such radical procedures as hemimandibulectomy to control the lesion. Radiation therapy is probably contraindicated. Although a cause-and-effect relationship obviously is not proved, the present series contains one example of a giant-cell reparative granuloma treated by radiation in which a lethal sarcoma developed subsequently in the same site. We are not aware of an instance in which spontaneous malignant transformation of giant-cell reparative granuloma has occurred.

Inadequate treatment had commonly been employed initially elsewhere in the present series, usually on the basis of an erroneous clinical diagnosis. The frequency of such inadequate procedures as dental extraction or "draining" of the region adjacent to the lesion with failure to recognize the basic underlying pathologic factors is to be condemned. The number of errors will be decreased if oral surgeons will depend on roentgenograms and routine submission of tissue to the pathologist for histologic analysis.

SUMMARY

In a study of benign multinucleated-cell-containing lesions of the jaws, sixty-four examples of giant-cell reparative granuloma and only two of genuine

giant-cell tumor of bone were encountered at the Mayo Clinic in a fifty-two-year period. Other benign giant-cell-containing lesions, such as aneurysmal bone cysts, cherubism, fibrous dysplasia, and malignant tumors, must be distinguished from giant-cell reparative granuloma.

The central and peripheral tumors of this giant-cell reparative process are so similar histopathologically that differentiation must be made on roentgenographic or surgical findings, and an arbitrary designation is sometimes necessary.

Giant-cell reparative granulomas respond favorably to conservative surgical removal, which is the treatment of choice.

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PREFABRICATED RADIOPAQUE SUTURES IN DUCTAL SIALOLITHOTOMY

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THE rationale, efficacy, and technique for the use of radiopaque suture material (a silk suture saturated with a contrast medium, Ethiodol) in the surgical treatment of small sialoliths in Wharton's duct has been described previously.[1] However, mention had been made of the possible benefits to be derived from a prefabricated suture material embodying a metallic core (radiopaque suture, Ethicon, Inc., New Brunswick, New Jersey). The purpose of the present article is to demonstrate the applicability of such a product in the localization and surgical removal of diminutive salivary stones involving the floor of the mouth. A brief review of the procedural steps and the inclusion of two illustrative case reports should adequately serve this purpose.

PROCEDURE

In order to overcome the problems encountered in a freely movable, three-dimensional soft-tissue area, such as the oral floor, the introduction of localizing and immobilizing sutures prior to surgery is mandatory. The insertion of radiopaque ligatures anterior and posterior to the sialolith satisfies these prime requirements.

The plica sublingualis approximating the posteroanterior course of the submaxillary duct and the initial occlusal x-ray film serve as guides for the proper positioning of the sutures. The radiopacity inherent in these sutures is utilized to confirm the accuracy of placement.

The appropriate placing of the posterior ligature is accomplished by introducing the suture needle and the attached thread (silk braided about a metallic core) through the mucous membrane of the floor of the mouth. The initial insertion commences at a point posterior to the stone and approximately 0.5 cm. medial to the plica. The needle is then carried deep to Wharton's duct emerging once again approximately 0.5 cm. lateral to the plica. An occlusal roentgenogram taken at this time will determine whether repositioning of the suture is necessary. Once the posterior tie has been installed, it is a relatively simple matter to insert the anterior suture by a similar technique. The occlusal film is once again utilized as a means of confirmation.

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The posterior suture then is tied tightly, constricting the submaxillary duct to prevent the stone from slipping backward, whereas the anterior suture may be only loosely applied. When the sutures are left sufficiently long, the tissues of the oral floor can be raised and made taut to facilitate dissection,

With the limits of the operative site circumscribed, the stone's position confined, and the soft tissue raised and immobilized, the operator is now in an advantageous position to commence the actual procedure of surgically isolating the involved portion of Wharton's duct via blunt dissection. Once the duct has been segregated surgically from the surrounding soft-tissue bed, a longitudinal incision is made into the duct to deliver the sialolith.

CASE 1.—J. G., a 26-year-old white woman, was referred because of the presence of a salivary stone in the right Wharton's duct.

There was a one-year history of recurrent swellings of the right submaxillary gland area. One month prior to examination, there had been an unsuccessful attempt to remove the calcification. An occlusal roentgenogram revealed the presence of a 5 mm. radiopaque mass at the junction of the middle and posterior thirds of the duct (Fig. 1).

Fig. 1.—Preoperative occlusal view revealing presence of small sialolith.

Clinically, the right submaxillary salivary gland was palpable but nontender. Intraorally, the floor of the mouth appeared normal without any evidence of inflammation.

As a preliminary step, the posterior limiting radiopaque ligature was inserted and its position was checked with an occlusal film (Fig. 2). The anterior tie was similarly placed, and its location was confirmed (Fig. 3). Both insulated metallic-core sutures were tied, and the tissues of the floor of the mouth were elevated by the application of tension (Fig. 4).

An incision 1.5 cm. in length was made through the mucous membrane of the right floor of the mouth, extending between the two confining sutures. The incisional line was designed to run immediately lateral and parallel to the plica sublingualis. By means of

blunt dissection in a medial and slightly inferior direction, the duct was visualized, exposed, and isolated with a heavy silk ligature (Fig. 5). A longitudinal incision through the superior aspect of the exposed duct permitted the liberation of the miniature sialolith (Figs. 6 and 7).

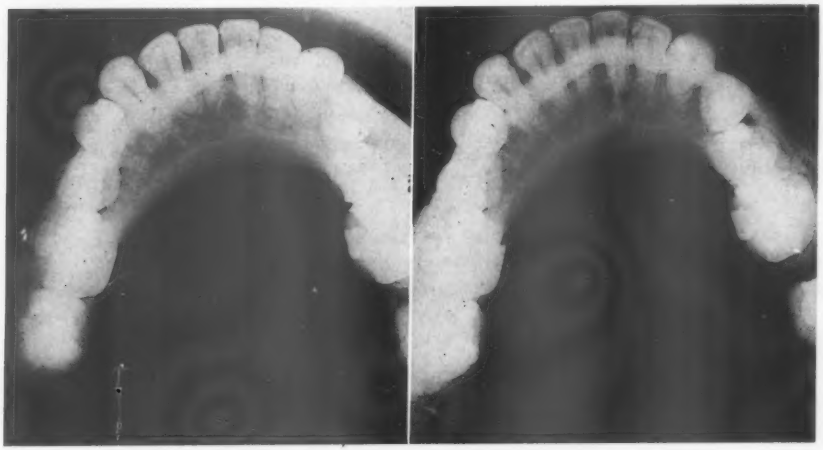

Fig. 2. Fig. 3.

Fig. 2.—Posterior radiopaque suture in position.
Fig. 3.—Anterior and posterior radiopaque sutures in position.

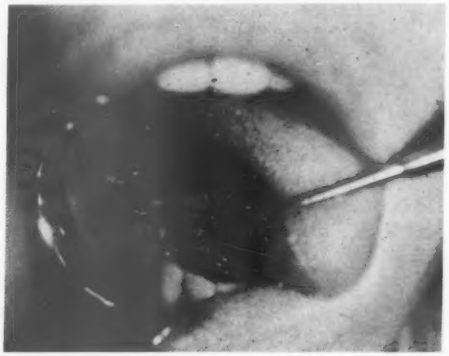

Fig. 4.—Intraoral view revealing positioning of anterior and posterior radiopaque sutures. Note application of tension in order to make operative field more accessible.

CASE 2.—M. K., a 50-year-old white man, was referred because of an acute right submaxillary sialadenitis and an associated sublingual abscess.

Questioning elicited no information concerning any previous episodes related to a salivary gland obstruction. An occlusal roentgenogram demonstrated the presence of a sialolith, approximately 6 mm. in diameter, situated in the middle third of the right Wharton's duct (Fig. 8).

The patient's acute symptoms were controlled by means of intraoral incision and drainage and antibiotic therapy. One week following the subsidence of the acute exacerbation, surgical removal of the causative stone was undertaken. As a preparatory step, the

Fig. 5.

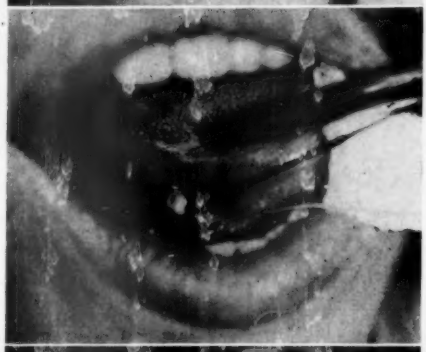

Fig. 6.

Fig. 7.

Fig. 5.—Operative view. Wharton's duct isolated by black silk suture. Note presence of anterior and posterior radiopaque sutures.

Fig. 6.—Operative view. Spontaneous extrusion of sialolith following incision into the duct. Note presence of black silk suture circumscribing the duct.

Fig. 7.—Postoperative occlusal view.

two localizing radiopaque sutures were inserted and tied (Fig. 9). Following this, a 2 cm. incision was made through the mucous membrane, lateral to the plica and within the area outlined by the anterior and posterior ligatures. Blunt dissection was successful in isolating the right Wharton's duct, which then was incised longitudinally so as to evacuate the entrapped sialolith (Figs. 10 and 11).

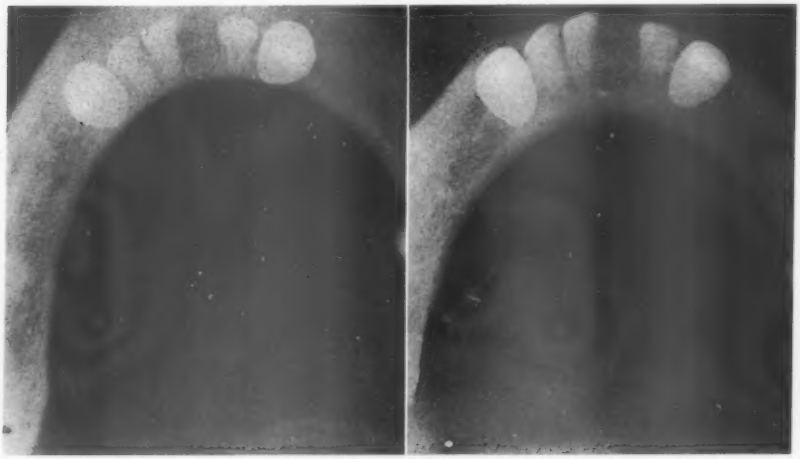

Fig. 8 Fig. 9.

Fig. 8.—Preoperative occlusal view revealing presence of small sialolith.
Fig. 9.—Anterior and posterior radiopaque sutures in position.

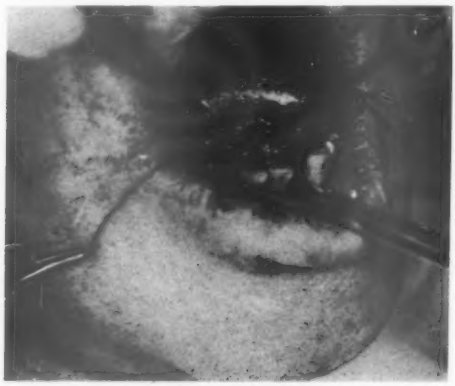

Fig. 10.—Operative view. Wharton's duct circumscribed, isolated, and raised by black silk suture (arrow).

COMMENTS

It is obvious that the utilization of the outlining radiopaque sutures is a vital step in the surgical approach to small, nonpalpable stones in the oral floor. This simple and relatively atraumatic preparatory procedure returns a dividend over and above the additional time consumed.

When the suture needle is introduced initially at the medial aspect of the plica, the possibility of injury to the blood vessels is minimized. It is true that the major vessels and nerves are, for the most part, located medial to the posterior portions of the sublingual gland and submaxillary duct, but at the same time the best and most accurate control of the needle is obtained during the first half of its introduction into the tissues.

Fig. 11.—Postoperative occlusal view.

The silk-braided wire suture appears to have a definite superiority over plain wire ligature. The ease in handling the suture, both during insertion and during the procedure, the ability to tie knots tightly without slippage, and the opportunity to apply external tension without tearing the enclosed soft tissues are all obvious advantages. With such excellent qualities, this prefabricated insulated wire ligature can be applied usefully to aid in the localization of other calcifications, roots, and foreign bodies in and about the oral cavity.

SUMMARY

The indications for the utilization of a prefabricated silk-braided wire suture (Ethicon, Inc.) in the surgical treatment of salivary stones of the oral floor have been discussed.

Two case reports have been presented, to demonstrate the successful application of this radiopaque suture material.

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800 GRAND CONCOURSE.

COMPLICATIONS ENCOUNTERED IN THE TREATMENT OF CANCER OF THE MOUTH

Thomas J. Cook, D.D.S., Miami, Fla.

IN 1952 I reported on a series of cases showing the effect of irradiation on unprotected teeth and their supporting structure following the treatment of cancer of the oral cavity.[1]

Following the publication of my article, I received several letters from radiologists. Some stated that they had treated many cases without complications, and others described a method of protecting the teeth.

The following case is submitted because of the complications which followed the surgical treatment of carcinoma of the floor of the mouth in an edentulous patient.

CASE REPORT

On June 26, 1953, a 59-year-old white woman was referred to my office by a fellow dentist. The patient was a fine-looking woman and in good spirits. She stated that she was wearing dentures and that she first noticed an ulcer under her tongue in April, 1953.

There was a lesion which could be seen when the patient removed her lower denture; it was in the midline and measured about 1 cm. in diameter. The mandible was not involved.

With the patient's consent, a biopsy was performed, and the pathologist reported squamous-cell carcinoma, grade 2. The nature of the report was discussed with the patient. She asked that we call her sister, who lives in a northern city, and explain it to her. The sister felt that the patient, who was alone, should go to her home so that she could be near her during the treatment period.

On July 28, 1953, the following report was received from a surgeon in the northern city:

"We did a fulguration and removal of the area from the floor of the mouth and the base of the tongue plus bilateral suprahyoid lymph node dissection and the tumor was removed in toto and there were many negative lymph nodes with no positive involvement.

"Mrs. _____ suffered a postoperative vascular accident in the left area which unfortunately has involved most of her speech center. This probably followed ligation of the external carotid which we do routinely in all procedures about the base of the tongue.

"The pathological diagnosis was: 'Squamous cell carcinoma of floor of mouth. Seven negative suprahyoid lymph nodes. Two negative submaxillary glands. Slight fibrosis and chronic inflammation of sublingual glands.'"

A letter from the patient's sister, dated July 30, 1953, read as follows:

"Dear Doctor:

"I have been intending to write to you concerning my sister's operation since you asked me to let you know the outcome, but unfortunately there have been complications and my time has been rather filled.

"We saw Doctor _____ in _____ and he advised immediate surgery. We also saw Doctor _____, whom you may know about. His advice differed rather widely, as he thought he would prefer to put radium seeds in the tumor for 30 days, then wait another 30 days before operating. The delay we all felt would be very hard for my sister to take, and she was strongly in favor of Doctor _____'s method. She had the operation last Friday morning. After a three-hour wait the doctor came and reported to me that she was fine and that he was pretty sure that he had 'got it all.' Of course that was very cheering news to me, as she had been so fearful that after the first operation there might be others to face. After about two more hours, when she was, I suppose, in the recovery room, she was brought down to her room, still unconscious. I was there until 8:30 that night, hoping that I could be on the spot whenever she did regain consciousness, but she did not. The next morning I went down early, and after Doctor _____ had seen her he came back and told me that she had apparently had a stroke, as she was still not conscious and her right arm and leg seemed to have no movement. I had noticed that she kept the right arm completely still all afternoon on Friday, but of course it didn't have any significance to me.

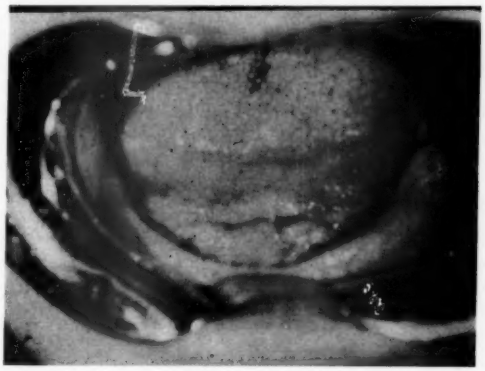

Fig. 1.—Photograph of tumor before biopsy.

He told me that this quite often happens in just this kind of operation with extensive surgery and said something about the large artery in her neck or throat or somewhere. I am sorry not to be more intelligent about just what happened, but you will doubtless understand, as he says it occurs in quite a large percentage of such operations in people over 50. I have never happened to hear of it and nobody with whom I have talked, except perhaps the nurses, have ever known of such a case. I got three nurses for the first 24 hours, before I knew the complications, but of course I have had to keep them on. The doctor thought we could let the 3 to 11 P.M. one go, so for the last two days I have taken over those hours. The reason for constant watching is, of course, the tube in her windpipe, as well as the feeding tube in her nostril. Her left hand unconsciously goes up to her throat, the dressings, etc., so automatically that we would be in trouble if someone were not with her at all times. We do restrain the left wrist lightly so that if the nurse has to turn away she is safe, but activity is coming back in her right arm now so that I feel someone has to be there about every minute. The action in the right leg is slower in returning, but there has definitely been some improvement in the last few days. Also, she now opens her eyes more frequently,

but unless I overwork my imagination I can't see any recognition. As far as I can find out from the doctors they really can't tell the duration of this thing. I suppose each case is different, so it is most unsatisfactory and worrying.

"You will be glad to know that apparently Dr. -------- is quite definite about his getting all the malignancy, as a doctor friend of ours called him and talked at length about the details which, of course, I can't understand in medical terminology. Although it was firmly attached to the jawbone and Dr. -------- said a piece of the bone would have to be removed causing considerable disfigurement, etc., this was not considered necessary by Dr. -------- and did not have to be done. He did tell me that some ridge will have to be rebuilt in order for her to wear her denture, but I think he meant that that was in front, though I may be wrong. Her tongue is wired up at present for some reason—perhaps this will give you some idea of the extent of the operation.

"I am very grateful to you for urging her not to delay and also for advising coming here where we could help her and be with her. I know that you understood what was before her, and our great regret is that she didn't go to you immediately when Dr. -------- advised her. But she had such confidence in Dr. --------, whom she has had for many years, that she went to him first, as you know. We can't understand how he could have failed to foresee the possibilities in such a case, and why he 'laughed her off' and gave her shots of penicillin instead of suggesting a biopsy. His failure has had tragic consequences because the surgery six months earlier might have been much less extensive and perhaps this vascular 'accident' would not have occurred.

"The incision has healed in fine shape, they tell me, and all the stitches and clips are out already. The only bright spot I can see in the whole picture is that by being unconscious so long she has been spared some of the extreme discomfort, pain, etc., which usually follows surgery. It is too high a price to pay, but it is a crumb of comfort to me.

"The expense of the nurses is, of course, terrific, and a great worry to us, as she cannot afford anything like it and although I could help her and would, for a while, the uncertainty of her future makes me feel that I should make my own funds last as long as possible. The doctor and the hospital have been most understanding and cooperative and will do what they can for her to ease the financial burden, and if she would only regain consciousness things would be much simpler. I forgot to say that a neurologist has been seeing her since they knew about this stroke condition, but I haven't been able to see him as yet, so don't know what he thinks except that he agrees with Dr. -------- and thinks she will gradually regain use of her limbs. I haven't yet dared ask if they can tell if there is any brain damage. I don't believe they can tell yet, anyway.

"I am sure I am missing many points in which you would be interested. The glands were involved, I believe, but not down in the neck; just under her chin, I think. The incision reaches almost from ear to ear, but I believe that the center part will be under her chin and not too noticeable, and the two ends will doubtless clear up as scars always do and finally fade out pretty well.

"In spite of great apprehension, she displayed wonderful courage before the operation. If she is faced with any incapacity I don't know whether she can take it or not, as she has to earn her own living and has had such a struggle for the last ten years or so that I fear for the consequences in that situation. But she knows she is welcome here and we give her the best care when she gets to the point of recuperating.

"Thank you so much for your interest. If you have any technical questions I would be glad to get answers from the doctor for you.

"Sincerely,

(Signed) --------"

I received a second letter from the patient's sister, dated Feb. 3, 1955:

"Dear Doctor:

"I am glad to bring you up to date on my sister, but very sorry that I have such bad news of her.

"She had been getting along fairly well at the Rest Home where she has been since September, 1953. She had gotten over the depression as far as one could tell, and did not cry for months, at least when I was there and as far as the nurses could tell. Her spirit has been wonderful under the very trying circumstances of her handicaps, though I am sure she had very little interest in life and had just resolved to put her best foot foremost and make it easier for us. I was able to get an occupational therapist from the National Association for Crippled Children and Adults (our local chapter) to come to see her and bring some handwork to fill some of her lonely hours. This proved to be a lifesaver for her and she has made dozens of woven pot holders, and even wove a scarf for her son, on a larger and more complicated loom. The work was perfect, and her use of colors and design excellent. I tell you this to show you how much she has improved and that she seems to be completely alert mentally, beyond the realm of words and speech.

"Around Christmas time she indicated to me that her mouth hurt her in some way. We thought it might be her denture, but examinations by her surgeon finally confirmed my fear that the cancer had returned. I am not entirely sure of the location, as the doctors use unfamiliar terms, but it is now in the jawbone as well as in her mouth. I took her to the x-ray therapy department of the -------- Hospital on the advice of her surgeon, and the specialist there told me at once that it looked pretty hopeless. They advised x-ray treatments, however, in the hope that they might retard the growth somewhat. I took her there every day for three weeks, ending last Saturday. Now she is to have a rest period, though it is far from that, as her mouth is very swollen and painful. They proceeded with the treatments very cautiously and, as I understood it, gave her less than in most cases, not wishing to make things worse, as is sometimes the case. They tell me that in a week or ten days the painful mouth should begin to be better. I sincerely hope so, as it is pitiful now, as she not only is uncomfortable but finds it very difficult to eat. Of course the medical doctor is giving her pain pills every four hours which are supposed to help, but of course do not eliminate the discomfort.

"Her lung x-ray was clear, they told me, and they seemed to think that the growth was confined to the mouth and jawbone. They may advise more x-ray treatments in a couple of months, after they see how things are. I am to take her to the hospital again on the 15th for an examination.

"It is a grim picture, and of course she is doomed eventually. I only hope she will not have to suffer too long. I go to see her every day now, though this fall I had to cut it down to every other day as it is quite a strain on me. Perhaps they can give me a little more idea of the future after they see the effect of the treatments. I am not sure but what the treatments cause more pain and discomfort than if they had left it alone. But of course I am in their hands, and they are doing their best to keep her as comfortable as possible. The aphasia makes it very difficult in so many ways, as we can't be sure whether she feels worse or better, since she cannot express herself. If she had been able to talk normally I can imagine that I could have made quite a pleasant life for her, but this cuts her off from everyone except the people at the home and my family. She enjoys her radio but has never been too keen about watching television, as it necessitates her being in the sunroom with the other patients, and I can easily understand that, as she was always very shy and retiring.

"This fall I began to take her to a Rehabilitation Center near us, run by Dr. -------- and Dr. --------. They felt they could help her in some measure and very soon advised having her long brace cut off below her knee. This gave her less support for walking at first, but she soon strengthened the big muscles above her knee, and with a cane and someone's arm she was able to get out and down the steps and into my car two or three times

a week. Of course, we have discontinued all that since the treatments began, as she has enough to endure without more physical effort. If things settle down to less pain perhaps we can begin them again, as I think it gives her something to do and is good for her to see how many crippled people of all ages come to the Center.

"I still feel that her doctor in --------, to whom she went first, was greatly at fault not to suspect or at least order a biopsy as a precaution, because taken at the very first the results might have been very different. I wrote him a factual letter after her operation with the hope that in similar cases he would take all precautions, and he apparently was very resentful of my writing as I did. He replied with a very nasty letter, criticizing my sister as a neurotic, etc., etc., and his story of his treatment of her mouth tumor was quite unlike hers. I have no reason to doubt my sister's story of his giving her a shot of penicillin and calling it a cyst. On the other hand, he states that he wanted to do a biopsy but that she begged off on account of funds. Perhaps this is true although she did not say so. I don't doubt that he was easy on her with his charges, as he says, and for that I should give him due credit. He says he referred her to Dr. -------- and, after consulting with him, 'we decided that she was a bad surgical risk, and offered to keep the growth under surveillance for her. Then the next thing we know or hear about her is from you.' Somewhere along the line there was a fatal delay. My sister may have been difficult—she had had an unbelievably hard life with her second husband, from whom she finally got a divorce—but I think that if they made such an important decision her family should have been notified or something done to help her. But perhaps I expect too much of doctors! I should say that I did not answer his letter as there was no point in doing so.

"I am sorry this has been such a long letter, but it is a very tender subject with me, and when I get started explaining her situation I write much too fully, I feel. But you asked for it! And I do appreciate more than I can tell you your interest in her case.

"Sincerely,

(Signed) --------"

COMMENT

The patient mentioned in this report went to her physician in April because of a lesion in the floor of the mouth and received antibiotic therapy. When the lesion did not respond to treatment, she went to see her dentist in June. A biopsy was performed, and after the pathologist's report was received the patient's sister was contacted and a plan for treatment was put into effect immediately.

Unfortunately, complications developed. The patient became a cripple, and her family became greatly inconvenienced and financially embarrassed because of a long period of hospitalization.

It is natural to assume that if the operation had gone well and the period of convalescence had been uneventful, everyone concerned would have been quite happy. However, the treatment for cancer is not always like that.

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1. Cook, T. J.: Late Radiation Necrosis of the Jaw Bones, J. Oral Surg. 10: 118, 1952.

5515 Orduna Dr.

A CASE OF FIBROMATOSIS GINGIVAE

Manawel Araiche, D.D.S., and Herbert Brode, D.D.S.,* Rochester, N. Y.*

DIFFUSE fibromatosis is a rare condition of gingival hyperplasia which usually manifests itself at the time of eruption of the permanent dentition. Fibromatosis affecting the deciduous teeth is a still more rare condition. A report of such a case follows.

CASE REPORT

The patient, a 4-year-old retarded white girl, was referred to the oral surgery department of Strong Memorial Hospital because of her progressive inability to eat any solid or soft foods. Oral examination showed diffuse hyperplasia of the entire gingivae, both buccally and lingually, on the maxilla. The incisal edges on the upper anterior teeth only were apparent (Fig. 1).

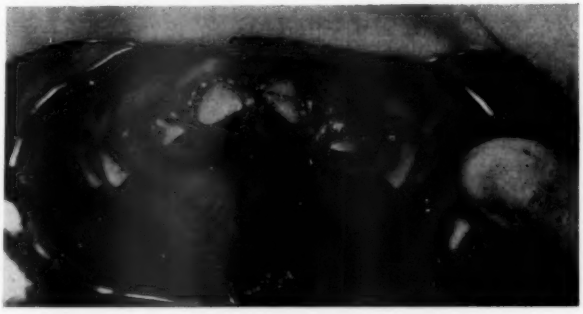

Fig. 1.—Patient's condition at referral.

History.—The child's parents stated that her teeth began to erupt at the age of 8 months. However, by the time she was 2½ years old there had been little or no progress in the eruption. Four dentists were consulted. They advised gingival massage, which was of no avail. A year later the dentist referred the patient to a pediatrician, who suspected hypothyroidism and admitted her to Strong Memorial Hospital for study.

Family history showed that no member of the family had any hyperplasia of the gingivae or retardation of eruption; moreover, the patient had two sisters who were normal. The patient's past history included the usual childhood diseases plus pneumonia at the age

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of 2 years, accompanied by one convulsion. The results of a complete physical examination, including protein-bound iodine and hemocytologic studies, were essentially normal except for the bone age, which was one and one-half years behind the chronological age according to the Greulich and Pyle standard, and the child's failure to respond to sound. Maxillary and mandibular films showed that the deciduous and permanent teeth were present and complete in number; no pathology was seen. The diagnosis was idiopathic mental deficiency associated with hyperplastic maxillary gingivae. It was decided to perform a gingivectomy on the maxilla.

Fig. 2.

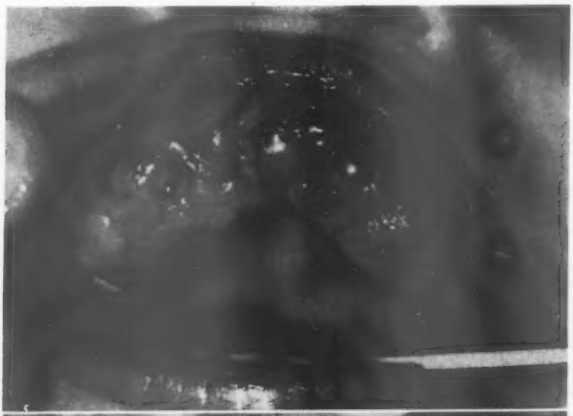

Fig. 3.

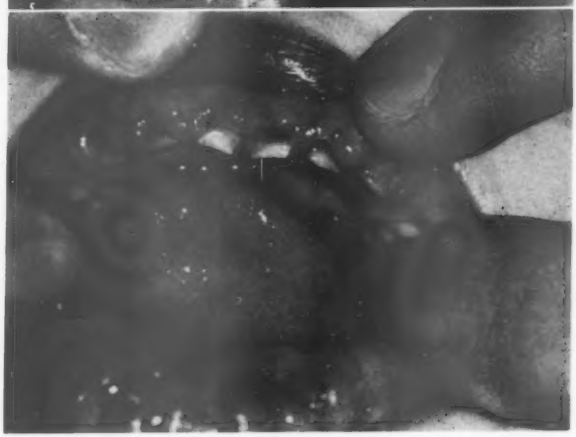

Fig. 2.—Patient's condition fourteen months after first excision of maxillary gingivae.
Fig. 3.—Patient's condition fourteen months after first excision of madibular gingivae.

On Dec. 6, 1956, an upper gingivectomy was performed with little difficulty. Hemorrhage was minimal, and the patient was discharged without any postoperative complications. The pathology report revealed fibromatosis gingivae. The parents were informed that the condition might recur.

Fourteen months later the patient returned with profuse overgrowth of both maxillary and mandibular gingivae (Figs. 2 and 3). The patient was admitted to the hospital for a

second gingivectomy. We decided to extract the upper anterior teeth, which were in labioversion. During the procedure profuse hemorrhage occurred, and one unit of blood was administered. There were no postoperative complications (Figs. 4 and 5). The pathology report was as follows:

Gross: The specimen, received in fixative with source of tissue being "gingivae," consisted of multiple fragments of white fibrous tissue with irregular edges, the largest measuring 3 by 0.4 by 0.4 cm.

Fig. 4.

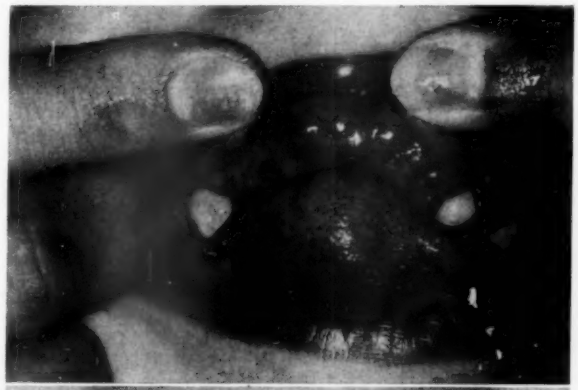

Fig. 5.

Fig. 4.—Postoperative result (maxilla).
Fig. 5.—Postoperative result (mandible).

Microscopic: The section showed stratified squamous epithelium covering a dense fibrocollagenous connective tissue stroma. The epithelium was thickened in some areas and had elongated narrow rete pegs. There were focal infiltrates of chronic inflammatory cells in the upper submucosa. Small areas of ulceration were seen, with denudement of the epithelium. The crater of the largest was filled with fibrin, and many surrounding acute and chronic inflammatory cells were seen. In another area there was a marked acanthosis and extension into the submucosa of rete pegs composed of large cells. There was an accompanying infiltrate of chronic inflammatory cells.

Diagnosis: Fragments of hypertrophied gingiva showing focal ulceration, fibrosis, chronic inflammation, and pseudoepithelial hyperplasia.

Two months postoperatively, at a regular checkup, a slight proliferation was noted. The condition seems to be recurring, and it will not be long before the child will have to undergo surgery again. No regrowth was noted in the upper anterior region where the incisors were extracted.

SUMMARY

A case of fibromatosis gingivae has been reported. After two gingivectomies, the condition appears to be recurring. Full-mouth extraction of the deciduous teeth will be envisaged the next time, giving the patient a period of relief before the eruption of the permanent teeth, as in most of the cases reviewed the hyperplasia is associated with the eruption of the permanent dentition. Radiation therapy was considered, but after consultation with the radiation therapy department it was dropped as ineffectual, if not harmful, since such treatment might affect any future surgical procedure on the bone and might possibly harm the development of the jaws.

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PERIODONTICS

. . . . . .

THE EFFECT OF COLD AS A STRESSOR AGENT UPON THE PERIODONTIUM OF ALBINO RATS

Gerald Shklar, D.D.S., M.S., and Irving Glickman, B.S., D.M.D., Boston, Mass.

WHEN the rat is exposed to cold for a lengthy period, there occurs a series of changes involving the endocrines and many of the metabolic systems influenced by them. Growth rate has been demonstrated to be adversely affected by exposure to cold during the first seven to ten days. Following this there was an increase in food intake and in body weight.[1]

Selye[2-4] found that cold was a severe stressor agent and used it routinely to elicit typical general adaptation syndrome changes, such as adrenal enlargement, thymicolymphatic atrophy, gastrointestinal ulcers, generalized tissue breakdown, and leukopenia. Selye also found that exposure to cold consistently produced typical general adaptation syndrome changes in the cardiovascular system.[4] Nephrosclerosis was often noted,[5] particularly in rats sensitized by unilateral nephrectomy as well as by high-protein and sodium-rich diet.

In studies on the alarm reaction, using formaldehyde injections as a stressor agent, we[6] observed degenerative changes in salivary glands but no notable gross or microscopic changes in the periodontal tissues. It was felt that the forty-eight-hour period of the alarm reaction was insufficient to produce changes in the periodontium. It was therefore decided to study the periodontal tissues in animals subjected to stress for longer periods of time. Exposure to cold was selected as the stressor agent.

EXPERIMENTAL PROCEDURE

Seventy young adult male albino rats, Wistar strain, aged 2 months and weighing 200 grams, were used. Thirty-five animals were maintained at a constant temperature of 0 to 2° C. for experimental periods of two weeks

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This report is from an investigation supported by the United States Public Health Service under Contract 646.

An abstract of this report was presented at the thirty-seventh annual meeting of the International Association for Dental Research in San Francisco, California, March 19-22, 1959.

(fifteen animals), one-month (fifteen animals), and four months (five animals). Thirty-five litter mates kept at 25° C. served as controls.

It was noted that the experimental animals drank less water and consumed approximately two and one-half times as much food. Both groups were fed Purina Chow. In the experimental animals there was a sharp drop in weight from 200 grams down to 100 to 150 grams at the end of two weeks. There was then a gradual weight increase, so that at the end of four months the weight of the experimental animals (300 to 350 grams) approximated that of the controls (350 to 400 grams).

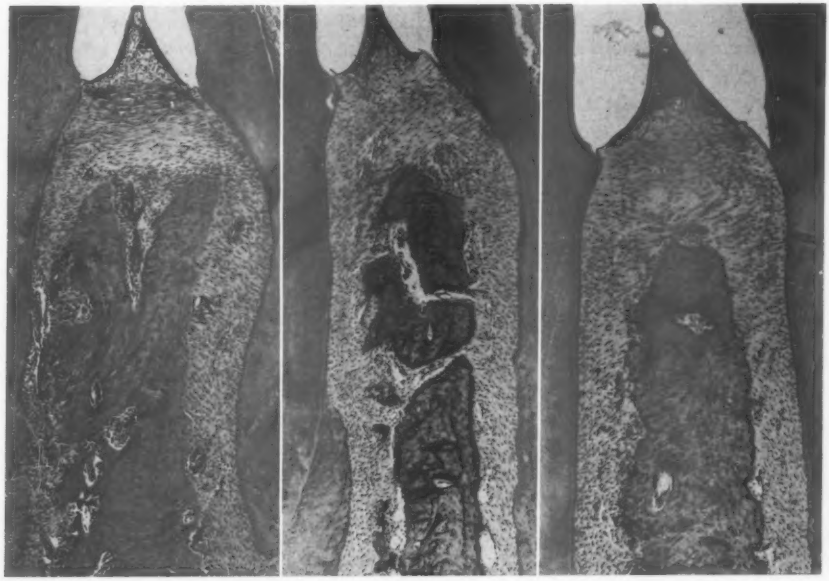


Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—Control animal (two-week experimental period). Mesiodistal survey section of the interdental septum area between first molar (left) and second molar (right). Note the scalloped mesial surface and the smooth distal surface of the interdental septum. (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅔.)

Fig. 2.—Cold-stressed animal (two-week experimental period). Mesiodistal survey section of the interdental septum area between first and second molars. Note the deeper stain at the distal margin. (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅔.)

Fig. 3.—Cold-stressed animal (two-week experimental period). Mesiodistal survey section of the interdental septum area between first and second molars. Note the sharply outlined distal margin of the septum. (Hematoxylin and eosin stain. Magnification, ×100; reduced ⅔.)

MICROSCOPIC OBSERVATIONS

Two-Week Experimental Period.—

Alveolar bone—interdental septum:

Control animals. The distal surface of the bone between the first and second molars was smooth in outline and was lined with a beadlike layer of

osteoblasts (Figs. 1 and 4). A layer of osteoid was noted at the surface, and some of the osteoblastic cells were partially embedded in the osteoid. The mesial surface of the septum presented an irregularly indented or scalloped outline. Occasional multinucleated osteoclasts were noted within lacunar spaces. The bone within the septum presented a homogeneous appearance in staining with lightly outlined apposition and resorption lines. The endosteal spaces were lined with osteoblasts. The crest of the septum tended to be rounded, and there was considerable osteoblastic activity present.

Cold-stressed animals. Changes were observed in all of the two-week experimental animals, but there was considerable variation in the severity of the responses. In the more severe cases, bone-formative activity was absent along the distal surface and the crest of the interdental septum. The distal surface was formed by a deeply staining margin devoid of osteoid or osteoblastic cells (Figs. 3 and 6). In less affected animals osteoblasts were present but in reduced numbers, and there was also some evidence of newly formed bone (Figs. 2 and 5). The bone within the septum presented a more irregular staining pattern than in the control animals. The apposition and resorption lines were more prominent, and the osteocyte lacunae stood out more sharply. In all animals in this group the number of osteoclasts usually found in the mesial surface of the bone was reduced. The crest of the septum appeared flattened in many of the experimental animals. The number of osteoblasts lining the endosteal margin was reduced.

Bifurcation area—interradicular alveolar bone:

Control animals. The interradicular bone between the mesial and distal roots of the first molar stained homogeneously. The surfaces of the bony trabeculae were lined with beadlike layers of osteoblasts and osteoid. The endosteal spaces were lined with osteoblasts (Figs. 7 and 9).

Cold-stressed animals. The interradicular bone stained more irregularly; the apposition and resorption lines and the osteocytes appeared more prominent. There was a reduction in the number of osteoblasts, but more notably in relation to the periodontal membrane than in relation to the endosteal spaces (Figs. 8 and 10). Osteoid formation was decreased.

Periodontal membrane:

Control animals. The periodontal membrane in relation to the interdental septa and the interradicular septa consisted of well-formed bundles of collagen fibers and numerous fibroblasts (Fig. 4). Many of the collagen-fiber bundles appeared to enter the bone and blend with the osteoid at the surface. The fibroblast nuclei were regular in shape and chromaticity.

Cold-stressed animals. The collagen appeared more granular than fibrillar. The fibroblasts were reduced in number and presented irregularities in distribution, size, and shape. The nuclei tended to be small and spherical, rather than elliptical, and deeply staining (Fig. 6).

Cementum: The number of cementoblasts and the amount of cementum apposition were diminished in the experimental animals.

Fig. 4.

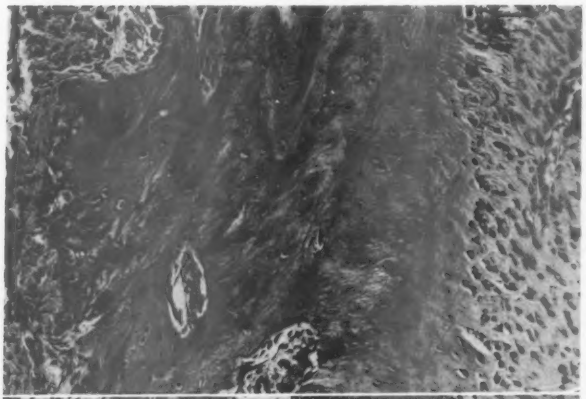


Fig. 5.

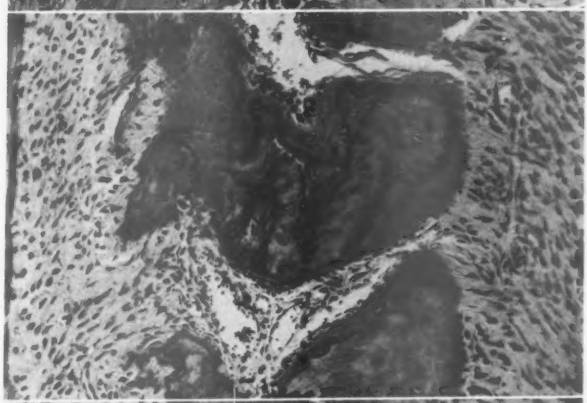
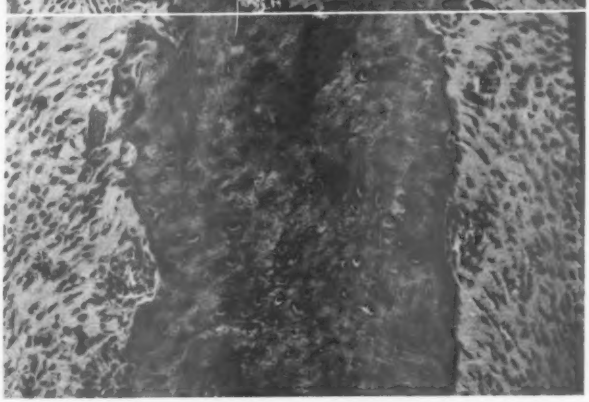


Fig. 6.



(For legends, see opposite page.)

Gingiva: No differences were noted in the gingival sulcus and in the epithelium of the attached gingiva of the experimental animals as compared with the controls.

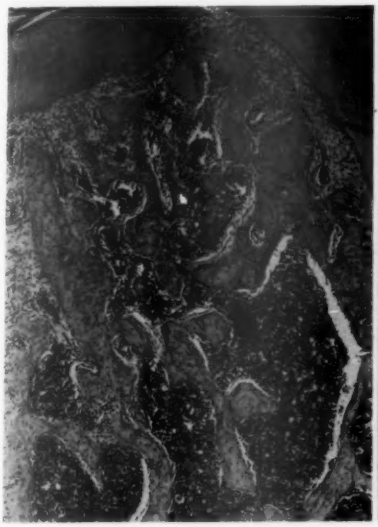


Fig. 7.

Fig. 8.

Fig. 7.—Control animal (two-week experimental period). Mesiodistal survey section of the interradicular bone between the mesial and distal roots of the first molar tooth. (Hematoxylin and eosin stain. Magnification, ×100; reduced 3/7.)

Fig. 8.—Cold-stressed animal (two-week experimental period). Mesiodistal survey section of the interradicular bone between the mesial and distal roots of the first molar tooth. (Hematoxylin and eosin stain. Magnification, ×100; reduced 3/7.)

Adrenal glands:

Control animals. The adrenal gland presented the usual demarcation of cortex into zona glomerulosa, zona fasciculata, and zona reticularis. The normal distribution of lipoid material was observed in the cells of the zona fasciculata.

Cold-stressed animals. The adrenal cortex appeared to be increased in width, and the demarcation of zona glomerulosa and zona fasciculata was not

Fig. 4.—Control animal. Detailed section of Fig. 1 showing the mesial (left) and distal (right) surfaces of the interdental septum and periodontal membrane. Note the regular distal surface covered with osteoid and lined with a beadlike layer of osteoblasts, the continuity of collagen fibers extending from the bone into the periodontal membrane, and the osteoclasts lying in lacunar spaces along the mesial margin of the bone. (Hematoxylin and eosin stain. Magnification, ×280; reduced 3/7.)

Fig. 5.—Cold-stressed animal. Detailed section of Fig. 2 showing the mesial and distal surfaces of the interdental septum and adjacent periodontal membrane. Note the accentuated staining of the incremental lines of the distal margin. There is a notable decrease in the number of osteoblasts along the distal surface of the bone. (Hematoxylin and eosin stain. Magnification, ×280; reduced 3/7.)

Fig. 6.—Cold-stressed animal. Detailed section of Fig. 3. Note the irregular somewhat scalloped distal margin of the interdental septum and the increased staining along the distal border. Note also the accentuation of the osteocytes with the large, sharply outlined lacunar spaces, as well as the complete absence of osteoblasts along the distal surface, the granular appearance of the collagen fibers, the reduction in the number of fibroblasts, and the decreased number of osteoclasts along the mesial surface. (Hematoxylin and eosin stain. Magnification, ×280; reduced 3/7.)

as clear-cut. There was a reduction in the amount of lipoid material in the zona fasciculata.

Salivary glands: In the experimental animals there were slight alterations in the sublingual and submaxillary glands, consisting of a diminution of

Fig. 9.

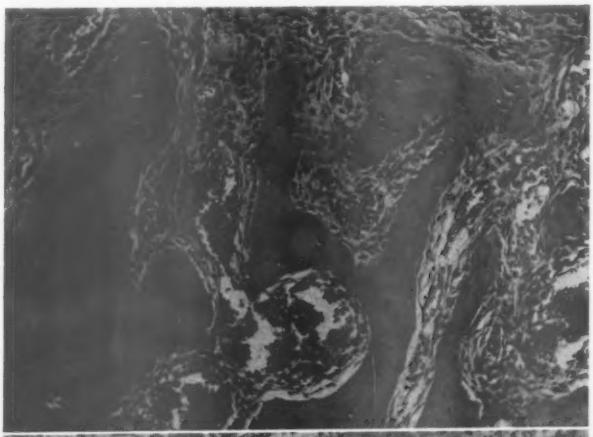


Fig. 10.

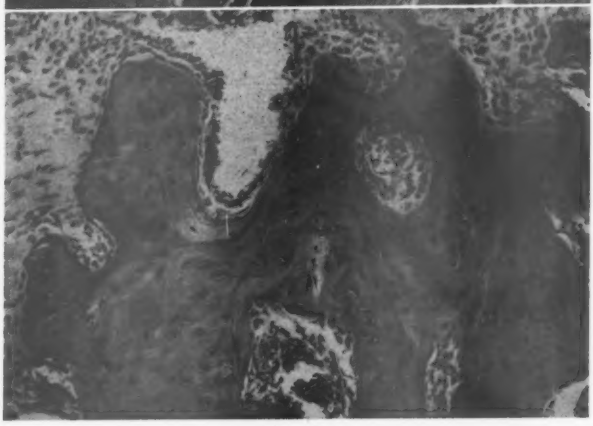


Fig. 9.—Control animal. Detailed section of Fig. 7 showing the abundance of fibroblasts and the beadlike layers of osteoblasts lining the bony spicules on both periodontal and endosteal surfaces. (Hematoxylin and eosin stain. Magnification, ×300; reduced ⅔.)

Fig. 10.—Cold-stressed animal. Detailed section of Fig. 8. Note the marked reduction in the number of osteoblasts and fibroblasts, particularly on the periodontal surface. (Hematoxylin and eosin stain. Magnification, ×300; reduced ⅔.)

basophilic material and cytoplasmic granules of the parenchymal cells. There was a reduction in the amount of interacinar connective tissue. The parotid gland presented no microscopic deviations from the normal.

Heart, lungs, liver, kidney, lymph nodes, and spleen: No notable alterations were noted in the heart, lungs, liver, and kidney. The lymph nodes and spleen presented a decrease in the density of the lymphatic cells.

Four-Week Experimental Period.—

Alveolar bone—interdental septum:

Control animals. The distal surface of the interdental bony septum between the first and second molars was smooth and regular in outline. There was a thick layer of osteoid in areas, as well as a beadlike arrangement of osteoblasts (Fig. 11). The osteoblasts were very much in evidence, although they

Fig. 11.

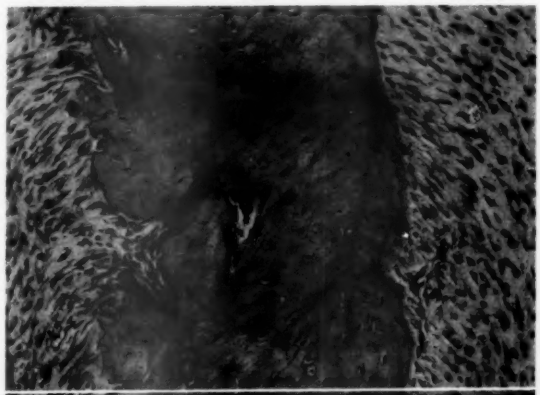


Fig. 12.

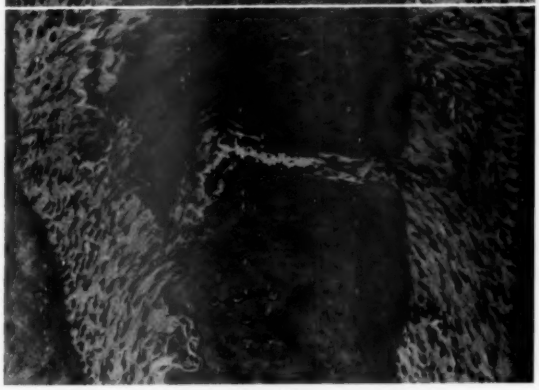


Fig. 11.—Control animal (four-week experimental period). Detailed area of the interdental septum between first and second molars. The area is similar to that in Figs. 4, 5, and 6. Note the layer of osteoblasts and the osteoid along the distal surface (right) of the bone. (Hematoxylin and eosin stain. Magnification, ×280; reduced ⅜.)

Fig. 12.—Cold-stressed animal (four-week experimental period). Detailed area of the interdental septum between first and second molars. Note the sharply accentuated margins of the bone and the decrease in the number of osteoblasts along the distal surface. (Hematoxylin and eosin stain. Magnification, ×280; reduced ⅜.)

appeared reduced in number as compared with the control animals of the two-week group. A large number of osteoblasts were often noted at the crest of the alveolar septum. The mesial surface of the septum presented a scalloped appearance with scattered osteoclasts lying in lacunar spaces.

Experimental animals. The number of osteoblasts and the amount of osteoid were reduced along the distal surface of the interdental septum (Fig.

12). The distal margin stained more deeply than in the control animals. The mesial surface of the septum presented an irregular, scalloped appearance with occasional osteoclasts. There was a reduction in osteoblastic activity at the alveolar crest. In general, the difference from the control animals was not as marked as in the two-week experimental period.

Bifurcation area—interradicular alveolar bone:

Control animals. The interradicular bone between the mesial and distal roots of the first molar presented a homogeneous staining with evidence of appositional lines. The bony crest and the distal surface of the bone were lined with osteoblasts, but the number of cells was reduced as compared with the control animals of the two-week period. The endosteal spaces were lined with osteoblasts.

Cold-stressed animals. There was an impression of reduced osteoblastic activity in this area in some of the animals, but the changes were not sufficiently notable to be definitive.

Periodontal membrane:

Control animals. The periodontal membrane in relation to the interdental septa and interradicular septa consisted of well-formed collagen bundles and numerous fibroblasts.

Cold-stressed animals. The collagen-fiber bundles appeared unaltered, but there was a reduction in the number of fibroblasts as well as a tendency for the fibroblast nuclei to be smaller and more darkly staining.

Cementum and gingiva: No notable alterations were noted in the cementum and gingiva of the experimental group as compared with the controls.

Heart, lungs, adrenals, lymph nodes, and kidneys: No notable changes were found in the heart and lungs of the one-month group. The adrenal glands presented slight evidence of cortical enlargement. The lymphatic tissue appeared normal. One interesting finding was related to the kidneys of the experimental animals. In several animals there was evidence of nephrosclerosis. This was found to be unilateral and varied in severity from complete necrosis and coagulation of glomeruli and tubules to slight regressive cellular alterations.

Four-Month Experimental Period.—There were no significant differences in the appearance of the periodontal tissues of the experimental and control animals.

DISCUSSION

In experimental animals subjected to cold, there was evidence of osteoporosis of alveolar bone and periodontal membrane changes consisting of a reduction in fibroblasts and a granular appearance of the collagen bundles. The osteoporosis varied in severity from a moderate reduction in osteogenesis to almost complete cessation of osteoblastic activity. Comparable changes were also present after four weeks, but they were much less severe. After four months the periodontium of the experimental animals was essentially normal.

The changes in the periodontium induced by exposure to cold may be explained in several ways. The adrenal cortical enlargement suggested that nonspecific stress, acting through the general adaptation syndrome, was of some importance. Another possible mechanism is that of a metabolic alteration so that nutrients required for tissue maintenance are consumed for the production of body heat. Decreased phosphorylative efficiency of mitochondria was found in animals exposed to cold,[7] and it was suggested that this could be a thermogenic mechanism which accounts for the conversion of energy.

It is interesting that the weight changes following exposure to cold paralleled the microscopic changes in the periodontium. The first two weeks were marked by weight loss and osteoporosis of alveolar bone. After the first two weeks the animals' weight increased until it was almost normal at the end of four months. The severity of the changes in the periodontium also diminished after the two-week period. By the end of four months the periodontium had returned to normal.

It would appear that exposure to cold is not an effective method for producing the exhaustion stage of the general adaptation syndrome. Adjustment occurs, minimizing the initial harmful effects.[8, 9] This was evidenced by the return of the adrenal cortex and periodontium to normal after four months.

SUMMARY

Exposure of male albino rats to temperatures of 0 to 2° C. for two weeks resulted in osteoporosis of alveolar bone, characterized by decreased osteoblastic activity and periodontal membrane changes consisting of decreased cellularity and granularity of the collagen. With continued exposure, the changes in the periodontium diminished in severity. There was evidence of changes after four weeks, but after four months the periodontium returned to normal.

We should like to thank Drs. Edward J. Masoro, James M. Felts, and Sylvia S. Lianides of the Department of Physiology, Tufts University, for their kind interest and advice.

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PERIODONTITIS SIMPLEX WITH OCCLUSAL TRAUMA

Report of a Case

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A 48-YEAR-OLD Negro housewife was admitted to this clinic with the complaint of pain and suppuration originating in the upper left quadrant. Examination of the area revealed severe mobility and supraeruption of the upper left second premolar. All teeth had heavy deposits of calculus, since the patient had never been treated by a dentist except for an earlier extraction in the lower right quadrant. Individual tooth mobility, height of the gingival margins, and depth of pockets were recorded.

The gingiva appeared pink and firm, but generalized recession with a texture loss of stippling was apparent. Prematurity of contacts was noted, with the lower left first premolar and first molar in a centric position; the lower left premolars and second molar and the lower right first and second molars in lateral excursion; and both upper central incisors in protrusion. Roentgenographic examination established the presence of a roentgenolucent area near the apex of the upper left second premolar, with much loss of lateral bone support. Also, progressive bone loss adjoining a multiple number of other teeth was verified. Intra-bony pockets were present on the mesial aspect of the upper right and lower left second premolars. Complete rehabilitation of the masticatory apparatus was initiated, since the patient expressed a sincere interest in her personal health and a willingness to cooperate.

The patient's history revealed no systemic disturbances or contraindications for dental treatment. Special laboratory tests and their results included the following:

Average saliva lactobacillus count—100 colonies per cubic centimeter.
Blood count—no abnormalities present.
Urinalysis:

Reducing sugar—negative.
Protein—tract.
Specific gravity—1.021.

Treatment.—The loss of bone support, with pain and suppuration, necessitated extraction of the upper left second premolar. All teeth were then scaled,

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curetted, filed, and polished. This was supported with instructions for the home care of teeth and supporting tissues.

Occlusal equilibration in centric, lateral, and protrusive positions was accomplished to eliminate prematurities. Since the patient admitted clenching and grinding the teeth, a bite plate was made and worn only at night. Gingivectomies with attempts at reattachment within intrabony pockets were comcompleted on the mesial aspect of the upper right and lower left second premolars. Missing teeth were replaced with bridges in the upper left and lower right quadrants. The mouth was again checked for occlusal equilibration and adjusted as necessary.

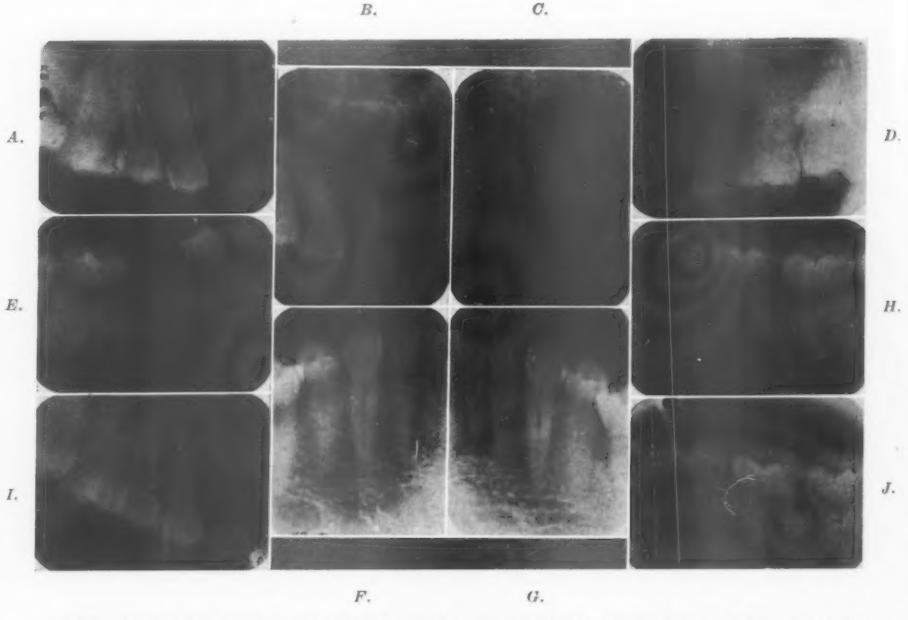

Fig. 1.—Roentgenograms *A* through *H* (all except those in the lower right- and left-hand corners) indicate the status of the teeth and supporting tissues before rehabilitation was initiated. *A* represents the upper right premolar area, and *H* shows the lower left premolar area. Roentgenograms *I* and *J* show these respective areas one year later, after gingivectomy and curettage.

Results of Treatment.—The thorough scaling and polishing of teeth augmented a return of stippling to the gingiva, along with a general reduction in pocket depth. Occlusal equilibration produced a complete and simultaneous contact in centric position and during jaw movements, thereby reducing premature stresses with tooth mobility. The patient indicated that the stiffness and tiredness of the jaws in the morning were no longer present since she had been wearing the bite plate. This remained true even when the wearing of the bite plate was reduced to every other night. Subsequent roentgenographic examination indicated that the subgingival curettage produced a significant

amount of reattachment. Placement of bridges in the two edentulous areas maintained the continuity of both arches and resulted in effective transmission of occlusal stresses.

The author expresses his appreciation for the instruction and assistance given by Drs. Bennett Klavan and Leo Sreebny, Department of Applied Materia Medica and Therapeutics, in the treatment of this case.

ORAL MEDICINE

LABORATORY TESTS FOR DENTISTS

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EVERY patient who places himself under the care of a dentist is a potential bearer of any disease known to man. Many of these diseases are diagnosed through information derived from laboratory tests. In hospital work particularly, a knowledge of these tests is essential, but many of them can be performed in the dental office on an outpatient basis. The literature is filled with laboratory experiments, but it is difficult to find in a condensed form a brief outline of tests which dentists may be called upon to use. I have therefore attempted to list these tests with such information as is of special interest to the dental diagnostician.

I. HEMATOLOGY

A. *Counting.*—

1. *Red Blood Cells.*—The normal values vary from 4,500,000 to 6,000,000 erythrocytes per cubic millimeter, being lower in women and children than in men.

Principle: Blood is diluted with an isotonic solution, and the red blood cells are counted in a hemocytometer chamber under a microscope.[1]

The red cell count is increased in primary polycythemia vera and secondary polycythemia (heart disease, pulmonary disease, and conditions resulting in decreased oxygen tension of the blood, that is, arteriovenous fistula, high altitudes, etc.). It is decreased in most anemias.

Comment: From the most reliable estimates, the standard of error of the red cell count lies between 8 and 10 per cent.[2]

2. *White Blood Cells.*—The normal count is 5,000 to 10,000 cells per cubic millimeter.

Principle: Blood is diluted with acid stain which lakes the red cells and stains the white cells.

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The white cell count is high in the presence of most inflammatory and toxic processes (pyogenic infections with staphylococcus and streptococcus), leukemic processes, and trauma (including bone fractures). It is low in the presence of specific infections (such as typhoid fever), and it is notoriously low in aplastic anemia and drug intoxication.

Comment: Persistent and severe leukopenia necessitates a thorough hematologic investigation, as it may indicate systemic disease or bone marrow damage. The same applies to a leukocytosis.

3. *Thrombocytes (Platelets).*—The normal range number is from 200,000 to 500,000 per cubic millimeter.

Principle: The blood is diluted with a fluid containing preservative and an anticoagulant and then stained with methylene blue.[3]

Interpretation: This test is often used for discovering thrombocytopenic purpuras whose only symptoms have been inexplicable gingival bleeding and/or oral petechiae in areas not normally traumatized. It is also a simple and inexpensive method of following the progress of thrombocytopenic purpuras, aplastic anemia, and leukemias after treatment has begun.

The platelet count is raised in polycythemia, after splenectomy, following severe hemorrhage, and in the presence of leukemia. It is lowered in cases of thrombocytopenic purpuras, severe infections, late leukemia, and aplastic anemia.

Comment: If thrombocytopenia exists, then operative procedures should be deferred until adequate platelets are present. A severe persistent thrombocytopenia is a sign of systemic disease and deserves further hematologic study.

4. *Blood Smear for Differential Count.*—

Method: A drop of venous blood is dropped onto a clean slide and spread across with another slide having the drop in back of a sweeping stroke. It is dried and stained with Wright's stain.

Interpretation: In a differential count, the predominant leukocyte and its relative maturity may be noted; the size, shape, maturity, and capacity of the red blood cells can also be evaluated. Normal white cell values are as follows:[4] neutrophils, 54 to 62 per cent; lymphocytes, 25 to 33 per cent; immature leukocytes (bands), 3 to 5 per cent; monocytes, 3 to 7 per cent; eosinophils, 1 to 3 per cent; and basophils, 0 to 1 per cent.

Mature and immature leukocytes may be identifiable in peripheral blood smears in the presence of leukemia and other hematologic disorders. An excess of a certain type of leukocytes can be a measure of disease, as shown in Table I.

Comment: Although classification is not complete, the value of the differential count cannot be overemphasized. Both total and differential white counts are excellent tools in following the course of the diseases listed in Table I.

B. *Hemoglobin Determination.*—The normal value is 14.5 grams per 100 ml., but values of from 11 to 18 are considered within the normal range.

Principle: The test utilizes the photoelectric method or the colorimetric system, both of which register the color intensity of the blood.

Interpretation: The test is an indication of the oxygen-carrying capacity of the blood, and it is sufficient to say that it is low in all anemias (secondary or primary) and high in the same conditions in which the erythrocyte count is elevated. The value should not be expressed in percentages.

TABLE I

NEUTROPHILIA	LYMPHOCYTOSIS	MONOCYTOSIS	EOSINOPHILIA	BASOPHILIA
Pyogenic infections (staphylococcal and streptococcal) Granulocytic leukemia	Lymphatic leukemia Infectious mononucleosis Whooping cough	Monocytic leukemia	Parasitic infections Eosinophilic granuloma (but not always present)	Polycythemia Basophilic leukemia

Comment: Surgery should be delayed when hemoglobin values fall below 10 Gm./100 ml.

C. *Hematocrit (Packed Cell Volume).*—The normal value is 35 to 50 per cent.

Principle: A fixed volume of whole blood is placed in a graduated tube and centrifuged, and the per cent volume of packed red cells is measured.

Interpretation: The packed cell volume is also a measure of the relative oxygen-carrying capacity of the blood, and the increased and decreased values in disease correspond to those of hemoglobin.

Comment: This test is easily performed and requires a minimal amount of equipment and technical skill. Values of less than 32 present a general anesthetic risk.

D. *Sedimentation Rate.*—This is expressed as the rate, in millimeters, at which the blood settles out after one hour, the normal being 3.7 mm. for men and 9.6 mm. for women, with a maximal range to 20 mm.

Principle: The test measures the velocity of erythrocyte sedimentation, this rate being increased in many diseases.

Interpretation: The sedimentation rate is nonspecific; there is a rise in the sedimentation rate in any disease in which there is inflammation, tissue degeneration, suppuration, or necrosis. It is useful in following responses to infections and in differentiating the neuroses from organic disease. If the patient is anemic, some authorities feel that a corrected sedimentation rate is necessary, but Wintrobe[5] believes that the correction of sedimentation rate should be abandoned.

E. *Bleeding Time.*—The normal range varies from one to six minutes.

Principle: This is a means of demonstrating the normal capillary function, and it is a reflection of the function and the number of platelets.[6]

Test: There are 3 types of tests—(1) the finger-tip pierce, (2) the ear-lobe pierce (Duke method) and (3) the Ivy method. The Ivy method is more time-consuming, but it is by far the most accurate.

Ivy method procedure: A cuff is placed on the forearm and inflated to register 40 mm. Hg, and the skin of the forearm is pierced with a 4 mm. hemolet. The drops of blood are absorbed away with filter paper at thirty-second intervals until bleeding has ceased.

Interpretation: A short bleeding time is of no clinical significance. The test should be discontinued at the end of fifteen minutes in those patients in whom there are no signs of cessation at that time, as further bleeding adds no additional information and has a bad psychic effect on the patient.[7] Bleeding time is prolonged in cases of thrombocytopenia, hereditary capillary defects, and defects in platelet function.

Comment: Bleeding time is normal in hemophilia and related diseases.

F. *Capillary Fragility Test (Rumpel-Leede's Test).*—

Principle: This test is nonspecific for capillary resistance and involves an increase in the hydrostatic pressure of the capillaries.

Test: A tourniquet is adequate, but an inflated cuff is desirable for standardization. The cuff is inflated to a point midway between systolic and diastolic pressure. If petechiae appear before ten minutes, the test is reported as positive. The test is positive in thrombocytopenia, capillary purpuras, scurvy, and senility.

G. *Clotting Time (Coagulation Time).*—The normal is eight to twelve minutes.

Principle: This is simply a test-tube test for the blood's ability to clot. There are two types of tests—(1) the capillary tube method, which employs a skin capillary and is generally considered unsatisfactory, and (2) the Lee-White method, which utilizes venous blood and is the more accurate.

Procedure: Venous blood, 1 c.c., is placed in three test tubes wet with saline. The first tube is tilted gently at thirty-second intervals until blood no longer flows down the side of the tube; then the thirty-second tilting is begun on the next two tubes in succession until clotting occurs. The time at which blood clots in the last tube, beginning from the time blood was removed from the vein, is reported as the clotting time.

Interpretation: An increased value indicates a clotting defect, but a normal test does not rule out the possibility of the patient's being a bleeder. The clotting time is increased in AHG, PTC, and PTA and a deficiency of the stable and labile factors; fibrinolytic disease; and hypothrombinemia.

Comment: The clotting time is normal in thrombocytopenia.

H. *Clot Retraction.*—Normally, clot retraction begins in thirty to sixty minutes and is complete in twenty-four hours.

Principle: The "pulling away" or retracting of a clot in a test tube varies in health and disease.

Interpretation: The beginning of clot retraction is established when a visible dimpling of clot surface occurs with extrusion of a tiny droplet of serum and is complete when the clot is distinct from the serum. The same tubes that are used for estimation of clotting times may be used for this test. The test is dependent upon blood platelets and plasma-coagulation factors. The character of the clot should also be noted, as a poorly formed, friable clot is an indication of disease.

Clot retraction is prolonged in thrombocytopenic states and liver disease.

Comment: This test is normal in patients with hemophilia and related diseases, even though their clotting time is prolonged.

I. *Prothrombin Time.*—The normal is thirteen to fourteen seconds.

Principle: Prothrombin is a carbohydrate containing protein formed in the liver; vitamin K is necessary for its synthesis.

Interpretation: The test utilizes all other clot mechanism factors (calcium, thromboplastin, etc.) in correctly established amounts, leaving prothrombin as the only variable. This test, the one-stage method of Quick, measures the entire clotting process except for the platelet hemophiliac factor; consequently, the result is normal in hemophilia and related bleeding diseases.[9]

Prothrombin time is prolonged in the presence of cirrhosis and any obstructive jaundice where vitamin K formation is impaired, following trauma of surgery with blood loss (death may be due to acute prothrombin loss), and in cases of deficiency of the prothrombin complex.

Comment: This test is of value in following patients who are receiving anticoagulant therapy with the coumarin group of drugs (Dicumarol).

J. *Prothrombin Consumption (Serum Prothrombin Time).*—

Principle: Normally, in clotting, prothrombin is almost completely consumed (80 to 90 per cent), leaving serum with little residual prothrombin. If there is a deficiency of thromboplastin in the blood, consumption of prothrombin is diminished, leaving a high prothrombin residual in the serum.[10]

Principle of the test: The amount of prothrombin converted into thrombin and the amount of residual prothrombin that remains in the serum after coagulation vary with the amount of thromboplastin and prothrombin that is available.

Interpretation: A serum prothrombin time greater than twenty seconds is normal, indicating that most of the prothrombin has been used. A value lower than this indicates that an abnormal amount of prothrombin is removed.

Prothrombin consumption is abnormal or decreased in AHG, PTC, and PTA deficiency, thrombocytopenic states, and deficiency of the accelerator substances.

K. *Antihemophiliac Globulin, Plasma Thromboplastin Antecedent, Plasma Thromboplastin Component Differentiation.*—AHG deteriorates after forty-eight hours in plasma, and PTA and PTC do not. Of the remaining two, PTC is absorbed by barium sulfate whereas PTA and AHG are not. With this principle, therefore, these three states can be identified.

II. BLOOD CHEMISTRY

A. *Blood Urea Nitrogen (BUN).*—The normal value is 9 to 19 mg. per 100 ml.

Principle: Urea is the end product of protein metabolism. Titration is the preferred method for its determination.

Interpretation: These values are raised in severe renal disease and lowered in pregnancy and malnutrition.

Comment: NPN tests which arrive at essentially the same information should be eliminated in lieu of the BUN test.

B. *Total Serum Protein.*—This is composed chiefly of albumins, globulins, and fibrinogens. The normal level is 6 to 7.8 grams per 100 ml.

Indications: The determination of total proteins supplies only limited information except in conditions of shock and dehydration, where concentrations increase, or in hemorrhage, where the level tends to decrease.[11]

Total serum protein levels are low in the presence of kidney disease, liver disease, malnutrition, and protein loss in hemorrhagic shock. They are high in cases of chronic infections, early liver disease, reticuloendothelial disease, and dehydration.

Comment: This test may be used as a guide in parenteral fluid administration in an emergency.

C. *Serum Glucose (Fasting Blood Sugar).*—The normal value is 80 to 120 mg. per 100 ml.

Principle: Titration or colorimetry may be used. This determination is primarily a test for diabetes, but it may also reveal other pathologic processes.

Serum glucose levels are increased in diabetes mellitus, acromegaly, adrenal tumors, anoxia (that is, in general anesthesia, tetany, and epilepsy), brain injuries, and chronic hepatic dysfunction. Serum glucose levels are decreased in diseases of the islets of Langerhans, hypopituitarism, and hypothyroidism.

Comment: Presumptive diagnosis may be made with values above 120 mg., but to confirm this diagnosis a glucose tolerance test may be necessary.[12]

D. *Carbon Dioxide (Capacity of Plasma).*—The normal is 25 to 31 mM per liter or 55 to 70 volumes per cent.

Indications: This test is used in cases of acid base imbalance.

Low carbon dioxide (acidosis) is found in hyperventilation (fever, hysteria, etc.), Addison's disease, diarrhea, intestinal fistula, and diabetic acidosis. High carbon dioxide (alkalosis) is found in pulmonary disease (from hypoventilation) and intestinal obstruction.

E. *Serum Chlorides.*—The normal is 570 to 620 mg. per 100 ml. (also expressed in milliequivalents).

Indication: This test should be performed when an electrolyte imbalance is suspected.

Serum chloride levels are raised in kidney disease, excessive IV saline, and dehydration and water loss. Lowered serum chloride levels are found in cases of vomiting and diarrhea and diabetic acidosis.

F. *Serum Sodium and Potassium.*—The normal value for potassium is 4.0 to 5.0 m.e. per liter, and the normal value for sodium is 138 to 145 m.e. per liter.

Principle: There are many methods, but flame photometry is the most accurate.

Interpretation: These tests are usually employed with the prolonged use of intravenous feedings or in the presence of any electrolyte imbalance.

Sodium deficiency is seen in cases of lowered intake, excessive perspiration, gastrointestinal discharge, kidney disease, and Addison's disease. Potassium deficiency occurs in cases of vomiting and diarrhea, diabetic acidosis, and overexcretion.

There is a sodium increase in overadministration of saline and in dehydration (more water loss than sodium loss). There is a potassium increase in excessive loss of chlorine as potassium chloride, heart failure and shock with tissue anoxia, adrenal cortical insufficiency, and excessive intake.

Comment: In general, it may be stated that values for serum potassium increase as values for sodium decrease.[13]

G. *Serum Calcium.*—The normal is 9 to 11.5 mg. per 100 ml.

Indication: Serum calcium should be determined whenever osteoclastic activity is suspected.

Serum calcium levels are reduced in hypoparathyroidism, bone disease, and vitamin D deficiency. These levels are elevated in hyperparathyroidism and hypervitaminosis D.

H. *Serum Phosphorus.*—The normal is 3 to 4.5 mg. per 100 ml.

Indications: In general, the indications for determining the serum phosphorus level are the same as for testing serum calcium.

Serum phosphorus levels are increased in nephritis, bone fractures, hyperparathyroidism, and osteoclastic bone metastasis and decreased in vitamin D deficiency.

Comment: This test is usually run in conjunction with the serum calcium test, as is the alkaline phosphatase.

I. *Alkaline Phosphatase.*—Alkaline phosphatase is the enzyme that splits the phosphate group in alkaline media. The normal value for adults is 1.5 to 4 Bodansky or 1.3 to 3.5 phenol units.[14]

High alkaline phosphatase levels are seen in the presence of any bone disease, osteoblastic activity, liver disease, Paget's disease, rickets, osteomyelitis, and hyperparathyroidism.

Comment: A lowered alkaline phosphatase has little or no significance.

III. URINE

A. *Examination.*—

1. *Volume:* The average normal volume is 1,500 c.c. in a twenty-four-hour period. Any variation from this may indicate renal, bladder, or prostatic disease. Variations also may include diabetes, blood-transfusion reactions, and shock.

2. *Specific gravity:* This may be conveniently established by the urinometer.[15] It is a measure of the relative amount of solids in solution and is indicative of the degree of tubular reabsorption. It varies inversely with the volume of urine excreted; therefore, renal damage usually may be ruled out if the specific gravity is high. In the presence of renal pathology, the specific gravity remains fixed. The normal is 1.029 to 1.032.

3. *Turbidity:* A cloudy white is usually a sign of pus in the urine, and a smoky red may indicate the presence of blood.

4. *Color:* The normal color is clear to yellow, and other colors are indicative of disease.

5. *Reaction:* Normal urine is acid in reaction and is influenced by diet. Urinary infections may produce an alkaline reaction. This test is easily and inexpensively performed with litmus paper.

B. *Microscopic Examination.*—

1. *Red blood cells:* Normally, a red blood cell appears per low-power field.

Abnormally high amounts are found in uncatheterized specimens taken during menstruation and in bleeding from the genitourinary tract (renal calculi, renal infarction, glomerulonephritis, renal malignancy, thrombocytopenic states, and trauma).

Comment: In continued sulfa therapy, the presence of red blood cells may indicate renal damage.

2. *Pus cells:* These may be seen in centrifuged urine in cases of urinary tract infection (pyelonephritis, cystitis, and urethritis).

3. *Epithelial cells:* A few normally exist per low-power field, and they are thought to be derived from the renal tubules, bladder, and renal pelvis.

4. *Casts:* It is normal for a few casts to exist. Abnormally high amounts are found in glomerulonephritis, heart failure, and some diseases of pregnancy.

C. *Urine Protein.*—This is chiefly a test for albumin, but some globulins do exist.

Usual procedure: Glacial acetic acid and water are added to urine. If the urine is cloudy, then albumin is present; the greater the cloudiness, the larger the amount of albumin. High amounts of albumin are found in febrile diseases, heart failure, kidney disease, urinary tract tumors, and malignant hypertension.

D. *Clinitest for Sugar.*—The commercial Clinitest tablet is dropped into 1 c.c. of urine, and 15 seconds after boiling it is read as follows:

Blue	Negative
Pale green	Trace
Green precipitate	1+
Green-yellow precipitate	2+
Yellow-orange	3+
Orange-red	4+

E. *Urine Sugar (Qualitative).*—Two methods are in wide use—Fehling's test and Benedict's test.

1. *Fehling's test:* Fehling's solution is added to urine and boiled. If the test is positive, the solution assumes an opaque yellow and red sediment forms at the bottom of the test tube.

2. *Benedict's test:* Benedict's reagent is added to urine, then boiled and cooled. The interpretation is made from the same colors and grading as in the Clinitest for sugar.

Interpretation: Other than diabetes, increased values are found in pancreatic disease, hyperthyroidism, pituitary disease, severe infections, and brain damage.

Comment: The presence of glycosuria is dependent upon (1) the concentration of carbohydrate in the blood, (2) the rate of glomerular filtration and (3) the degree of tubular reabsorption. The renal threshold is 160 to 180 mg. per 100 ml., and then sugar spills over into the urine.

F. *Urine Calcium Determinations (Sulkowitch Test).*—

Principle: This depends on the precipitation of calcium as insoluble calcium oxalate.

Method:[16] Urine and Sulkowitch reagent are mixed and allowed to stand two to three minutes and calcium precipitates out. The precipitate varies from a fine, white, cloudy appearance to a very heavy precipitate and may be graded 1, 2, 3, 4. A trace is normal.

Indications: A decalcification of previously normal skeleton may result in abnormal amounts of calcium in the urine. It is of prime importance in the study of bone disease.

The test is positive in hyperparathyroidism and in diseases in which there is rarefaction of the skeleton. It is negative in tetany, rickets, and sprue.

Comment: For best results, a number of specimens should be taken at different hours, since varying amounts are excreted in each voiding. It may also be of value to know the calcium intake.

SUMMARY

Twenty-nine tests in laboratory hematology, blood chemistry, and urinalysis are presented; some, such as the red and white counts, hemoglobin, urinalysis, etc., are used routinely, but others are less frequently employed. No new concepts are offered, but an attempt has been made to present, in a condensed, practical form, laboratory tests that are specifically useful for dentists in office and hospital practice.

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PHARMACOLOGY AND THERAPEUTICS

THIOSTREPTON, A NEW ANTIBIOTIC: TUBE DILUTION SENSITIVITY STUDIES

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With the Technical Assistance of Florence Funigiello

THIOSTREPTON[1-3] is a new and extremely active antibiotic derived from a strain of *Streptomyces azureus* isolated from a New Mexico desert soil sample.

This investigation of the sensitivity of various pathogenic microorganisms to a new antibiotic, Thiostrepton, was intended to parallel disc sensitivity studies with Thiostrepton which have been reported from this laboratory previously.[4] These preliminary studies, using discs impregnated with Thiostrepton, have indicated a probable spectrum of antibiotic activity for Thiostrepton that is somewhat like penicillin in range and potency. The tube dilution studies described herein are reported to offer further more detailed and more definite information with regard to the actual sensitivity (minimum inhibitory concentration) of microorganisms to Thiostrepton with particular emphasis on that portion of the spectrum against which Thiostrepton is most active as determined by previous preliminary screening with antibiotic discs.

Pagano and associates,[1] who first described Thiostrepton, have also studied the characteristics of the streptomyces species and described the solvent requirements of Thiostrepton, paper chromatography studies, agar diffusion and tube dilution assays, stability, and minimal inhibitory concentration of Thiostrepton against various microorganisms.

METHODS

Because of the marked insolubility of Thiostrepton[1] in aqueous solutions (without the inclusion of another specific solvent for Thiostrepton) which has been described previously, our technique for undertaking tube dilution studies was as follows: The antibiotic substance, Thiostrepton, was prepared as a

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Thiostrepton for this study was available through the courtesy of the Squibb Institute for Medical Research, New Brunswick, New Jersey.

solution in dimethyl sulfoxide. The material was then stored in polyethylene bottles at –30° C. In order to prepare the antibiotic for use in tube dilution testing, it was necessary to thaw the frozen stock solution by placing the polyethylene container in a beaker of water at 30° C. until thawing was complete. Antibiotic assay broth (Baltimore Biological Laboratory) was employed as the diluent and basic medium for these tests. One milliliter of the stock Thiostrepton solution was added to 100 ml. of antibiotic assay broth, resulting in a broth solution containing 2 mcg. of Thiostrepton per milliliter. In addition, this broth concomitantly contained 2 per cent of the solvent, dimethyl sulfoxide.

Sterile test tubes (15 by 100 ml.) covered with aluminum caps were used for sensitivity testing. To 0.5 ml. of the antibiotic-containing solution was added 0.5 ml. of a 1:100 dilution in broth of an eighteen- to twenty-four-hour culture of the test organism grown at 37° C. From this point, a standard serial dilution technique was performed so that the concentration in the tubes ranged from 1.0 to 0.00195 mcg. per milliliter in twofold steps. The final volume of each tube was 1.0 ml. A control tube for bacterial growth was included in each tube dilution series.

The series was incubated for twenty-four hours at 37° C., at which time it was examined macroscopically for evidence of growth. The lowest concentration of Thiostrepton which prevented growth was considered to be the minimal inhibitory concentration.

Ten strains of each group of microorganisms were isolated, cultured, and studied for sensitivity to Thiostrepton by the above-described tube dilution methods. The microorganisms thus studied included the nonhemolytic streptococcus, *Streptococcus hemolyticus, Staphylococcus albus, Staphylococcus aureus,* and selected other organisms. All organisms (except nine Group A hemolytic streptococci and seven miscellaneous organisms which were available as stock cultures through the courtesy of the New York State Department of Health) were obtained from pathologic materials submitted for bacteriologic study to the Department of Bacteriology of the New Rochelle Hospital. This material was obtained without selection from various areas of the body, including blood, urine, wounds, etc.

RESULTS

The results of the tube dilution studies (for twenty-four hours) appear in detail in Table I.

The minimum inhibitory concentration for Thiostrepton against the ten *Staphylococcus aureus* organisms tested ranged from 0.03 mcg. to 0.0035 mcg. per milliliter, with a median of 0.0150 mcg. per milliliter.

The minimum inhibitory concentration of Thiostrepton against the *Staphylococcus albus* organisms tested ranged from 0.0625 mcg. to 0.0156 mcg. per milliliter, with a median of 0.0312 mcg. per milliliter.

The minimum inhibitory concentration of Thiostrepton against the Group A *Streptococcus pyogenes* organisms tested ranged from 0.1250 mcg. to 0.0019 mcg. per milliliter with a median between 0.0039 and 0.0156 mcg. per milliliter.

TABLE I. MINIMAL INHIBITORY CONCENTRATIONS (TWENTY-FOUR-HOUR CULTURES) OF THIOSTREPTON FOR VARIOUS MICROORGANISMS

MICROORGANISM	LAB. NO.	SOURCE	MINIMAL INHIBITORY CONCENTRATION OF THIOSTREPTON BY VISUAL OBSERVATION AT 24 HOURS (MCG./ML.)
Staphylococcus aureus	3,294	Surgical wound	0.0150
	3,261	Surgical wound	0.0150
	3,255	Abscess of leg	0.0035
	3,276	Breast abscess	0.0070
	3,440	Nose	0.0300
	3,389	Tongue	0.0300
	3,241	Ear	0.0150
	3,306	Bone	0.0300
	3,289	Abscess, groin	0.0150
	3,304	Abscess, leg	0.0150
Staphylococcus albus	38	Ear	0.0312
	151	Nose	0.0625
	161	Abscess, hand	0.0312
	164	Blood culture	0.0625
	162	Rectal abscess	0.0625
	189	Furuncle, neck	0.0312
	197	Urine	0.0312
	352	Peritoneum	0.0625
	370	Abdominal fluid	0.0156
	402	Abdominal lesion	0.0312
Streptococcus faecalis	614	Throat	0.5000
	450	Feces	0.0078
	451	Throat	0.0156
	583	Urine	0.0625
	619	Throat	0.0125
Streptococcus mitis	654	Throat	0.0312
	572	Throat	0.0250
	695	Throat	0.0250
	619	Throat	0.5000
	620	Throat	0.0156
Streptococcus salivarius	691	Throat	0.0125
	687	Throat	More than 1.0000
Escherichia coli	3,758	Abscess, arm	More than 1.0000
		Urine	More than 1.0000
		Urine	More than 1.0000
Aerobacter aerogenes	3,754	Mouth	More than 1.0000
	3,761	Abscess, finger	More than 1.0000
	3,773	Feces	More than 1.0000
	3,780	Feces	More than 1.0000
	3,222	Urine	More than 1.0000
Salmonella typhimurim	3,681	Feces	More than 1.0000
Salmonella newport		Feces	More than 1.0000
Salmonella "C"		Feces	More than 1.0000
Salmonella typhimurim	40,141	Feces	More than 1.0000
Proteus rettgeri	3,820	Urine	More than 1.0000
Proteus mirabilis	3,920	Abscess, thigh	More than 1.0000
Proteus mirabilis	3,941	Pilonidal cyst	More than 1.0000
Proteus mirabilis		Vagina	More than 1.0000
Pseudomonas aeruginosa		Urine	More than 1.0000

TABLE I—CONT'D

MICROORGANISM	LAB. NO.	SOURCE	MINIMAL INHIBITORY CONCENTRATION OF THIOSTREPTON BY VISUAL OBSERVATION AT 24 HOURS (MCG./ML.)
Streptococcus pyogenes	831		0.0039
Group A varieties	32,369	Stock culture NYS Dept. Health	Less than 0.0019
	42,221	Stock culture NYS Dept. Health	0.0625
	41,470	Stock culture NYS Dept. Health	0.0156
	41,443	Stock culture NYS Dept. Health	0.0625
	41,459	Stock culture NYS Dept. Health	Less than 0.0019
	41,464	Stock culture NYS Dept. Health	0.0039
	165	Stock culture NYS Dept. Health	0.0312
	4,228	Stock culture NYS Dept. Health	Less than 0.0019
	334	Stock culture NYS Dept. Health	0.1250
Pneumococcus Type 1		Stock culture	Less than 0.0019
Type 2		Stock culture	Less than 0.0019
Type 3		Stock culture	Less than 0.0019
Corynebacterium xerose		Stock culture	Less than 0.0019
Bacillus subtilis		Stock culture	0.0156
Mycobacterium phlei		Stock culture	More than 1.0000
Neisseria catarrhalis		Stock culture	0.0312

The minimum inhibitory concentration for Thiostrepton against the *Streptococcus faecalis* organisms tested ranged from 0.5000 mcg. to 0.0078 mcg. per milliliter, with a median of 0.0156 mcg. per milliliter.

The minimum inhibitory concentration for Thiostrepton against the *Streptococcus mitis* organisms tested ranged from 0.5000 mcg. to 0.0156 mcg. per milliliter, with a median of 0.0250 mcg. per milliliter.

The minimum inhibitory concentration for Thiostrepton against the *Streptococcus salivarius* organisms tested was greater than 1.0000 mcg. per milliliter for one organism tested and 0.0125 mcg. per milliliter for the other.

A group of five organisms, including one each of pneumococcus Type 1, pneumococcus Type 3, *Neisseria catarrhalis*, pneumococcus Type 2, and *Corynebacterium xerose* were found highly sensitive to Thiostrepton.

A group of eighteen other microorganisms tested, including three *Escherichia coli*, five *Aerobacter aerogenes*, four salmonella species, four proteus species, one *Pseudomonas aeruginosa*, and one *Mycobacterium phlei* were all resistant to Thiostrepton in a concentration of 1 mcg. per milliliter.

As a further control measure to demonstrate that the results of these tube dilution studies should be attributed entirely to the antibiotic action of Thiostrepton rather than to any action of the solvent dimethyl sulfoxide, the following study was performed: Twenty-nine strains of *Staphylococcus aureus*, eight strains of *Staphylococcus albus*, six strains of *Streptococcus hemolyticus*, nineteen strains of *Escherichia coli*, five strains of *Proteus mirabilis*, nine strains of *Streptococcus faecalis*, twenty-three strains of *Streptococcus viridans*, eight strains of *Aerobacter aerogenes*, three strains of *Pseudomonas aeruginosa*,

two strains each of *Klebsiella pneumoniae* and *Neisseria catarrhalis*, and one strain each of *Candida albicans, Lactobacillus leichmannii, Bacillus subtilus, Sarcina lutea, Saccharomyces cerevisiae, Zygosaccharomyces prioranus*, and *Aspergillus niger* were individually inoculated into suitable broth media containing 1 per cent dimethyl sulfoxide (the maximum concentration of this solvent used in this study) and into unmedicated control media. In each instance, growth in the 1 per cent dimethyl sulfoxide media was equivalent to that in the unmedicated control media.

The above findings indicate that further laboratory and clinical studies with Thiostrepton are indicated.

DISCUSSION

Our study reinforces the tube dilution data orginally presented[1] with respect to Thiostrepton and suggests that the originally published preliminary data (obtained largely from stock cultures) was well within the spread of the minimum inhibitory concentration values within which it can be expected that microorganisms previously not exposed to Thiostrepton may be found.

The following data provide an indication of the relative activity[1] of Thiostrepton and other available antibiotics against a sensitive strain of *Staphylococcus aureus* (209P). The minimal inhibitory concentrations of various antibiotics against this *Staphylococcus aureus* strain (established by means of a tube dilution test using Penassay broth as the test medium) were as follows: Thiostrepton, 0.02 meg. per milliliter; erythromycin, 0.23 meg. per milliliter; carbomycin, 0.10 meg. per milliliter; penicillin, 0.03 units per milliliter; Streptomycin, 2.50 meg. per milliliter; tetracycline, 0.12 meg. per milliliter; bacitracin, 1.43 units per milliliter; neomycin, 0.53 meg. per milliliter; and gramicidin, 0.24 meg. per milliliter.

Further studies in our laboratory, which will be reported subsequently, suggest that microorganisms can develop resistance to Thiostrepton and, further, that this antibiotic has a bacteriostatic activity at and considerably above the minimal inhibitory concentration, rather than a bactericidal action.

In view particularly of the potency of Thiostrepton as indicated by the very minimal concentration of antibiotic required to arrest growth of many organisms, clinical trial on a topical basis with this antibiotic seems indicated in the treatment of infections caused by those organisms found sensitive to this antibiotic.

Workers intending to undertake tube dilution studies with Thiostrepton as above are cautioned that the toxicologic properties of dimethyl sulfoxide have not been fully investigated. Hence, ingestion of this compound or its prolonged contact with the skin should be avoided.

SUMMARY

Tube dilution studies concerned with Thiostrepton were performed on a series of strains of each of the following species of microorganisms: various nonhemolytic streptococci (twelve strains), hemolytic streptococci (ten strains),

Staphylococcus aureus (ten strains), *Staphylococcus albus* (ten strains), and seventeen other selected microorganisms.

Tube dilution studies with Thiostrepton against the above-mentioned organisms indicated a marked inhibitory capacity of this antibiotic in extremely low concentration against sensitive microorganisms. The minimum inhibitory concentration of Thiostrepton against the various microorganisms studied after twenty-four hours was as follows: For *Staphylococcus aureus,* a range of 0.0300 meg. to 0.0035 meg. per milliliter, with a median of 0.0150 meg. per milliliter; for *Staphylococcus albus,* a range of 0.0625 meg. to 0.0156 meg. per milliliter, with a median of 0.0312 meg. per milliliter; for *Streptococcus pyogenes* Group A, a range of 0.1250 meg. to 0.0019 meg. per milliliter, with a median of 0.0039 to 0.0156 meg. per milliliter; for nonhemolytic streptococci—*Streptococcus faecalis* (five strains), a range of 0.5000 meg. to 0.0078 meg. per milliliter, with a median of 0.0156 meg. per milliliter; for *Streptococcus mitis* (five strains), a range of 0.5000 meg. to 0.0156 meg. per milliliter, with a median of 0.0250 meg. per milliliter; for *Streptococcus salivarius* (two strains), a range of 1.0000 meg. per milliliter for one organism and 0.0125 meg. per milliliter for the other.

Eighteen other microorganisms tested, including three *E. coli,* five *A. aerogenes,* four salmonella species, four proteus species, one *Pseudomonas aeruginosa,* and one *Mycobacterium phlei* were resistant to Thiostrepton in a concentration of one meg. per milliliter.

Five organisms, including one each of pneumococcus Type 1, pneumococcus Type 2, pneumococcus Type 3, *Neisseria catarrhalis,* and *Corynebacterium xerose,* were found highly sensitive to Thiostrepton.

Further laboratory and clinical studies with Thiostrepton are indicated.

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THE INFLUENCE OF CONCENTRATION OF VASOCONSTRICTOR ON LOCAL ANESTHESIA

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RECENTLY there has been made available to the dentist one of the newer vasoconstrictors known as Neo-Cobefrin,* which is the levo isomer of nordefrin (Cobefrin*) in combination with the two local anesthetics Ravocaine* hydrochloride (propoxycaine hydrochloride) and Novocain* (procaine hydrochloride). Pharmacologic studies[1] in animals indicate that most of the biologic activity of nordefrin resides in the levo isomer. The dextro isomer is not entirely devoid of activity, however, being about 1/100 to 1/200 as active as the levo form. In addition, the activity which it does possess is longer in duration than that of the corresponding levo compound. The racemic compound, which of course contains exactly equal parts of the dextro and levo isomers, has long been used as a vasoconstrictor in local anesthetic solutions at a concentration of 1:10,000. It seems preferable to epinephrine for this purpose in that it produces fewer undesirable side effects on both the cardiovascular and central nervous systems. If only the pure levo form is used, it would be expected, on the basis of theoretical considerations, that the equivalent concentration would be 1:20,000. However, such an assumption cannot be accepted at face value without experimental evidence. The possibility exists that dextro and levo forms may act competitively on the cell receptors, so that the presence of the dextro isomer could in some way interfere with the action of the more potent levo form. Such an interference has been reported for the closely related vasoconstrictor synephrine.[2]

In view of the above considerations, it seemed desirable to undertake a clinical study to evaluate the effectiveness of several concentrations of Neo-Cobefrin in comparison with several other solutions of known clinical acceptability.

METHOD

All the solutions employed in this study contained Ravocaine hydrochloride 0.4 per cent and Novocain 2 per cent as the anesthetic agents. Three of the

*Trademarks of Sterling Drug Inc.

solutions contained Neo-Cobefrin as the vasoconstrictor at levels of 1:15,000, 1:20,000, and 1:30,000. For purposes of comparison, two other vasoconstrictors which have an extensive clinical background were used. Namely, Cobefrin, 1:10,000 and Levophed* 1:30,000 (levarterenol). It is seen, therefore, that the only variable in the five solutions was the vasoconstrictor.

In this study the "blind" method of Tainter and associates[3] was used in the course of routine private practice. The cartridges were so coded that the operator did not know which solution was being used. There was only one operator involved; therefore, all the observations were my own, and the same criteria were accordingly applied to all observations. The records were kept on cards like those reported by Dobbs and colleagues.[4] Three arbitrary grades of anesthesia were chosen: A, B, and C. Grade A was recorded in those cases in which there was complete freedom from pain. In Grade B the patient may have noticed some pain, but in the opinion of the operator reinjection was not necessary. Those cases in which sufficient pain was present to require reinjection were recorded as Grade C. The onset and duration times were recorded, as were immediate systemic and postoperative reactions. The systemic reactions included subjective ones, such as palpitation and others associated with apprehension. All were minor. The results are recorded in Table I as averages plus or minus the standard error of the average. The figures in parentheses give the number of patients for which that particular average was calculated. In those instances in which this figure is smaller than the total number of patients treated, the difference represents patients on whom observations were not made.

DISCUSSION OF RESULTS

It may be seen from the table that the solution which gave the highest incidence of Grade A or completely satisfactory anesthesia was the one containing Neo-Cobefrin 1:20,000, with considerably lower incidence being observed with some of the other solutions. The onset time with all the solutions was quite rapid and substantially equal, being on the order of one minute or less. Duration of anesthesia was longest with the solution containing Cobefrin, which is the racemic compound. This finding was not unexpected, since observations in animals reported by Luduena and co-workers[1] indicated that the dextro isomer had a very prolonged effect in comparison with the levo compound. Of the three solutions containing the levo form (Neo-Cobefrin), the longest duration was obtained with the 1:15,000 concentration, as was to be expected. The shortest duration would be expected with the 1:30,000 concentration, but the figures do not bear this out. Actually, the 1:30,000 concentration produced a slightly longer duration than the 1:20,000 concentration, although the differences are small and not significant statistically.

With regard to systemic reactions, Cobefrin produced the highest incidence and Neo-Cobefrin 1:20,000 the lowest. All three of the solutions containing Neo-Cobefrin showed a lower incidence of systemic reactions than did the racemic compound and were of about the same order of magnitude as the solution containing Levophed. The solution containing 1:30,000 Neo-Cobefrin would

TABLE I

SOLUTION	NO. OF PATIENTS	GRADE OF ANESTHESIA (PER CENT)				ONSET TIME OF ANESTHESIA (SECONDS)	DURATION OF ANESTHESIA (MINUTES)	MANDIBULAR ANESTHESIA (MINUTES)	INFILTRATION ANESTHESIA (MINUTES)	PER CENT WITH NO SYSTEMIC REACTIONS	PER CENT WITH NO POSTOPERATIVE REACTIONS
		A	B	C	NO INFORMATION						
RNN 1:15,000	81	96.3 ± 2.1	3.7 ± 2.1	0	0	54.0 ± 7.8 (78)	181.25 ± 6.61 (73)	202.45 ± 8.18 (29)	167.27 ± 9.00 (44)	91.4 ± 3.1	100.0
RNN 1:20,000	72	98.6 ± 1.38	1.4 ± 1.38	0	0	55.8 ± 7.2 (64)	164.05 ± 7.14 (59)	192.04 ± 12.61 (23)	145.14 ± 7.28 (35)	94.4 ± 2.7	100.0
RNN 1:30,000	57	91.2 ± 3.8	5.3 ± 2.97	3.5 ± 2.4	0	54.6 ± 8.4 (56)	169.93 ± 9.17 (54)	194.50 ± 21.84 (18)	155.19 ± 8.36 (32)	93.0 ± 3.4	100.0
RNL	86	88.4 ± 3.5	7.0 ± 2.8	1.2 ± 1.17	3.5 ± 1.98	60.6 ± 24.6 (33)	188.14 ± 9.10 (73)	209.70 ± 9.33 (23)	176.65 ± 12.87 (46)	91.9 ± 2.9	97.7 ± 1.6
RNC	77	92.2 ± 3.1	7.5 ± 3.0	1.3 ± 1.29	0	51.6 ± 6.0 (76)	193.31 ± 10.12 (67)	202.55 ± 15.35 (22)	173.53 ± 12.06 (38)	88.3 ± 3.7	97.4 ± 1.8

be expected to show the lowest incidence of systemic reactions, but this was not borne out by the data. It should be pointed out, however, that the differences in this regard between the three solutions containing Neo-Cobefrin are not statistically significant.

No postoperative reactions were observed with any of the solutions containing Neo-Cobefrin. They were seen in only two patients treated with Cobefrin and two patients treated with Levophed. The absence of edema, swelling, or soreness at the site of injection is noteworthy, but it should be pointed out that this is a reflection of the lack of irritation from the local anesthetics as well as the effectiveness of Neo-Cobefrin.

There appears to be an optimal concentration of vasoconstrictor for the local anesthetic agents used. Neo-Cobefrin 1:20,000 is the most satisfactory with the combination used in this study. When systemic and postoperative reactions are considered together, it appears that the solution containing 1:20,000 Neo-Cobefrin is better tolerated than those containing Levophed or Cobefrin. In addition, this solution also produces a higher incidence of Grade A anesthesia and a shorter duration. There was no indication from these clinical studies that the presence of the dextro isomer of nordefrin interferes in any way with the activity of the more potent levo form. However, there is some indication that it may modify the action by producing a slightly longer duration.

SUMMARY

A blind study on 210 office patients, selected at random, was undertaken to examine the relationship of the concentration of vasoconstrictor to the efficacy and duration of local anesthesia. Three concentrations of Neo-Cobefrin (1:15,000, 1:20,000, and 1:30,000) were used in combination with Ravocaine hydrochloride 0.4 per cent and Novocain 2 per cent. For purposes of comparison, the same anesthetic solution was also employed with Levophed and Cobefrin. Of the five solutions studied, the one containing Neo-Cobefrin 1:20,000 gave the highest incidence of completely satisfactory anesthesia, the shortest duration, and the lowest incidence of systemic reactions.

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ORAL ROENTGENOLOGY

American Academy of Oral Roentgenology

Arthur H. Wuehrmann, Editor

PERIAPICAL CEMENTOBLASTOMA

Report of a Case*

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PERIAPICAL roentgenolucencies often present great diagnostic problems. They may represent cementoblastomas, benign neoplasms made up of connective tissue generally of limited growth. They may be spoken of as cementifying fibromas. The lesions originate in the periapical region of the normal permanent dentition as a result of proliferation of cells of the periodontal membrane. In some instances the result is fibrous connective tissue containing foci of osteoid, while in others cementum is produced.

Stafne, in a large series of cases (10,000 consecutive adult patients), found twenty-four cases of periapical roentgenolucencies involving a total of fifty-two teeth. Prior to his examination, however, some of these patients may have had teeth associated with such areas removed on the assumption that they were granulomas or early radicular cysts. One can assume, therefore, that the incidence is at least two per 1,000 persons. The ages of the patients varied from 20 to 62 years. Seventy of the patients were women. Complete general physical examinations did not reveal any specific systemic disturbance that would account for resorption of bone. There were no patients with hyperthyroidism.

There are many instances in which the lesion remains very small and the roentgenopacity varies so little from the surrounding bony process that roentgenographic diagnosis is uncertain.

Differential diagnosis depends largely upon the stage of the development at which the periapical condition is observed and upon the clinical appearance of the involved teeth in association with pertinent history. The initial stage

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*First of a series of reports of unusual cases.

is the one which causes most confusion in diagnosis and the one at which most misinterpretations are made. Depending upon the size of the area, the periapical roentgenolucencies are invariably diagnosed as periapical infection or radicular cysts. The presence of roentgenolucent areas around the apex of a tooth which has normal color, positive vitality, and no history of trauma, pain, or pulpitis should suggest this growth to be a cementoblastoma. This is particularly true if the tooth involved is a mandibular incisor.

CASE REPORT

The case illustrated in Fig. 1 is that of a 43-year-old white woman with no pain symptoms. The teeth are normal as to color and vitality. There are no systemic complaints.

The case is illustrative of either multiple periapical cementoblastomas or cementomas, since considerable roentgenopaque tissue has been deposited (Fig. 1) about the apices of both maxillary anterior and mandibular anterior and posterior teeth. It is only very occasionally that this condition is seen about the apices of both the maxillary and mandibular teeth in the same mouth.

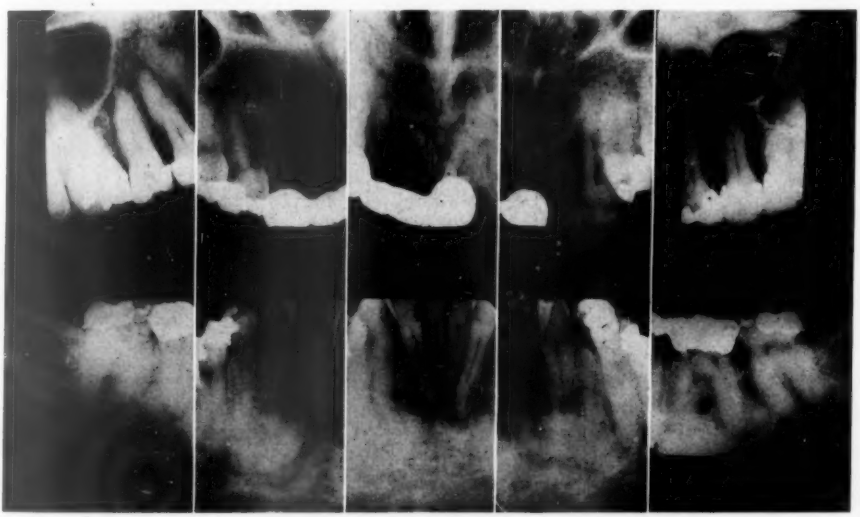

Fig. 1.

SUMMARY AND CONCLUSIONS

The occurrence of periapical roentgenolucencies in man is not as uncommon as formerly supposed. The significance of the lesion lies in the fact that it should be included in the differential diagnosis of apical pathology. In later development, roentgenopaque tissue is deposited while the growth usually remains relatively small and the teeth affected invariably remain vital. These roentgenopaque areas may attain large size, as in the case presented. Removal is rarely justifiable; this is particularly true if such removal involves the devitalization or loss of vital, healthy teeth.

ROENTGENO-QUESTIONS

Are the diagnostic qualities of a dental x-ray film in any way lowered when the film is exposed for a longer time and the developing time shortened to two or three minutes?

Any effort to speed up the process and reduce darkroom time results in lessened quality of the developed film. Film density results primarily from developing time and milliampere seconds (Ma.S.) of exposure. An underdeveloped film lacks detail because there has not been adequate time for the developer to reach and affect all the silver granules affected by the radiation. As a result, the fixer removes a lot of the latent images which the developer should have brought out; hence, there is a loss of detail.

Why do the faster dental x-ray films with emulsions on both sides of film base appear to have longer-scale contrast than the older, slower, and intermediate speed films, especially when exposure techniques up to 90 KVP are used?

Film speed can be increased by the manufacturer by increasing the size and/or number of the grains of silver in the emulsion, which makes the film more sensitive to smaller quantities of radiation.

Inherent in the qualities of the fast films, which are designed to reduce the amount of radiation used to expose the film, is that of long-scale contrast. This results in a roentgenogram in which the images of the dental structures of various densities show many shades of gray in the "color" spectrum, ranging from black to white, rather than in only a few shades of gray. It is possible, with proper techniques and kilovoltage control, to reveal slight and early changes in the dental tissues. Higher kilovoltages, even with intermediate-speed films, characteristically produce films with longer-scale contrast than relatively lower kilovoltages produce, because the higher kilovoltages produce more shorter wavelengths that increase the penetration of the tissues and hence impress more detail in the film emulsion.

The American Academy of Oral Roentgenology solicits from the readers of ORAL SURGERY, ORAL MEDICINE AND ORAL PATHOLOGY any questions which deal with technical or interpretive aspects of oral roentgenology. These questions should be sent directly to the editor of this section, Dr. Arthur H. Wuehrmann, School of Dentistry, University of Alabama Medical Center, Birmingham, Alabama; the editor will distribute them for reply to a suitable group within the Academy. Questions, with the answers, will be published at as early a date as possible in "Roentgeno-Questions." Questions, especially those of an interpretive nature, should ordinarily be accompanied by good-quality roentgenograms and a pertinent history. The names of the questioner and the respondent will not be published.

ORAL PATHOLOGY

A STUDY OF BONE LESIONS IN A CASE OF HYPERPARATHYROIDISM

B. Cohen, London, England*

A WOMAN, aged 48 years, was referred to the Dental Department at St. Mary's Hospital, Paddington, complaining of discomfort related to a small swelling in the left premolar region of the mandible. She was edentulous. A roentgenogram (Fig. 1) showed an area of rarefaction. When this was explored surgically under local anesthesia, it was found to be occupied by maroon-colored soft tissue of firm consistency. This was enucleated and diagnosed histologically as an osteoclastoma (Fig. 2).

Some two months later the patient returned complaining of discomfort caused by her lower denture. Swellings of the alveolar ridge were present bilaterally. Roentgenograms (Figs. 3 and 4) revealed extensive rarefaction bilaterally. The possibility of hyperparathyroidism was therefore investigated, and the patient was found to have a serum calcium level of 17.17 mg. per cent and a serum phosphate of 2.2 mg. per cent. Roentgenograms of the rest of the skeleton taken at this stage revealed only the earliest indications of osteoporotic changes.

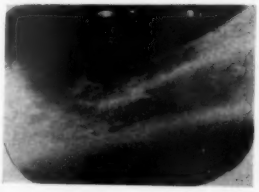

Fig. 1.—Intraoral roentgenogram of left premolar region taken on March 29, 1957.

An exploratory operation of the neck disclosed the presence of a parathyroid adenoma, roughly spherical in shape and measuring approximately 1.5 cm. in its greatest diameter (Fig. 5). At the same time a small thyroid adenoma of the left lobe was discovered and removed.

Postoperative recovery was uneventful, and the progress of healing in the mandibular lesions was followed by serial x-ray examinations (Figs. 6, 7, and 8).

Sixteen weeks after the parathyroidectomy the patient died. Death was found to be due to a cerebral hemorrhage. Histologic studies of the mandible provide the basis for this report.

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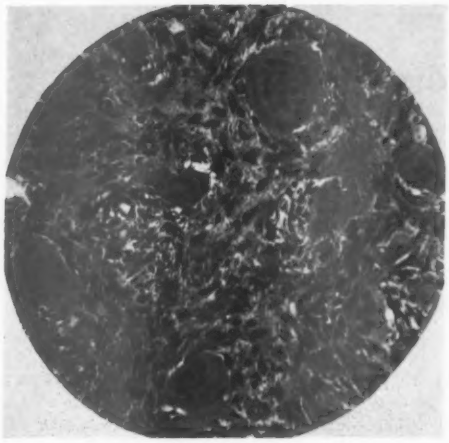

Fig. 2.—Biopsy specimen from area shown in Fig. 1. (Hematoxylin and eosin stain. Magnification, ×300; reduced ⅓.)

Fig. 3.

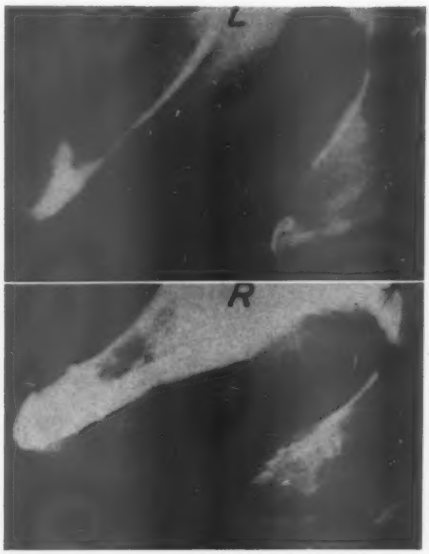

Fig. 4.

Fig. 3.—Lateral oblique roentgenogram of left mandible taken on July 1, 1957.
Fig. 4.—Lateral oblique roentgenogram of right mandible taken on July 1, 1957.

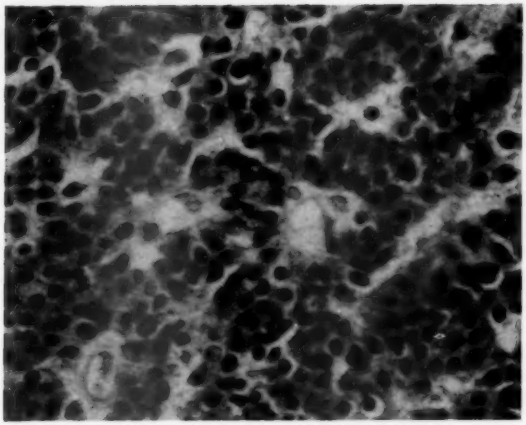

Fig. 5.—Parathyroid adenoma. (Hematoxylin and eosin stain. Magnification, ×450; reduced ⅝.)

Fig. 6.

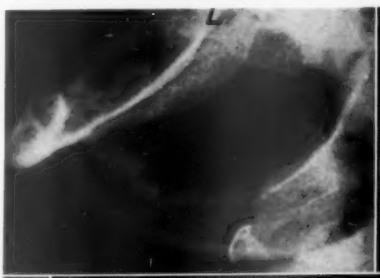

Fig. 7.

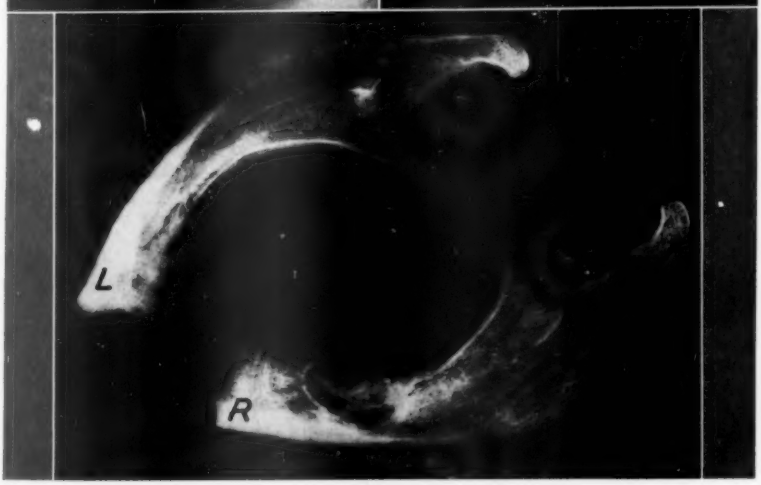

Fig. 8.

Fig. 6.—Lateral oblique roentgenogram of left mandible taken on Sept. 25, 1957.
Fig. 7.—Lateral oblique roentgenogram of right mandible taken on Sept. 25, 1957.
Fig. 8.—Left and right mandibular rami. Postmortem roentgenograms taken on Nov. 4, 1957. The soft tissues had been removed.

The material used had remained unfixed for approximately forty-eight hours post-mortem. It was then fixed in 10 per cent formol saline and subsequently decalcified in 10 per cent formic acid.

Fig. 9.—Enlargement of section through the lesion on the left side showing extensive repair. *L*, Lesion. (Hematoxylin and eosin stain. Magnification, ×12; reduced ⅔.)

Histology.—On the left side clinical and roentgenologic appearances (Fig. 8) had shown that healing was practically complete. Fig. 9 shows that the greater part of the area about the lesion had been replaced by new bone. In the small remaining foci of the lesion red blood cells, pigment, and giant cells could be detected (Fig. 10). None of these features is as well defined as those which appear in the larger lesion of the right side.

Fig. 11 shows the oral mucosa and the cortical bone of the lower border of the mandible to be intact on the right side. The lower portion of the mandibular ramus appears to have remained unaffected. Myeloid tissue, more often than not absent from the mandible in this age group, was present in this instance. The neurovascular bundle appeared to have been displaced downward by the original lesion, and the roof of the mandibular canal had

clearly been resorbed. The greater part of the cross-sectional area was the site of extensive repair. New bone had replaced the tissue of the lesion multifocally. Closer examination of the last remaining areas of the lesion reveals certain constant features. In no instance was new bone laid down in close proximity to giant cells. In every case these latter are disposed centrally in an area of free hemorrhage (Fig. 12). It is as though the giant cells had been herded to the center of a focus and the peripheral fibrous tissue, thus cleansed, had then become a suitable milieu for the encroaching process of ossification. However, should a less passive role for giant cells be envisaged, one might postulate that they were engaged in actively clearing extravasated red cells and other cell debris in advance of the new bone

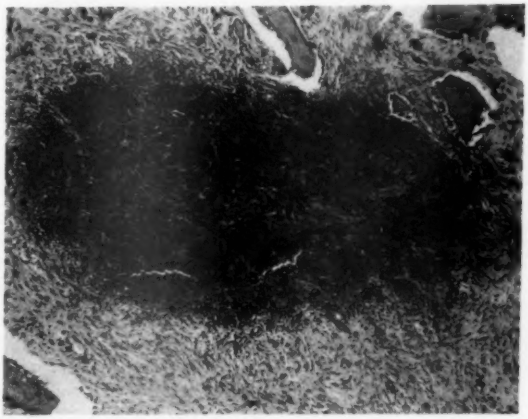

Fig. 10.—One of the last remnants of the lesion on the left side, showing active new bone formation surrounding a focus containing giant cells. (Hematoxylin and eosin stain. Magnification, ×120; reduced ⅝.)

formation. Apart from the formation of these central foci dominated by the presence of giant cells, some alteration was evident in the arrangement of the fibrous tissue from which they had migrated; there was a suggestion of bony trabecular pattern in the alignment of their formed elements (Fig. 13). Finally, at the periphery, active new bone formation was taking place circumferentially. Osteoblasts were not only numerous but appeared to be larger and more plump than those normally seen (Fig. 14).

DISCUSSION

The Giant Cells.—In addition to providing a narrative of the lesion's development and its healing postoperatively, the foregoing case throws light upon the nature and behavior of the giant cells seen in the bone lesions of hyperparathyroidism. There can be little doubt that these are true osteoclasts, to be distinguished from foreign body giant cells. The experiments of Weinmann and Schour[7] showed that the administration of parathormone to experimental animals led to the differentiation of osteoclasts and that these persisted after the microscopic disappearance of the bone to whose resorption they had been related. If, as seems reasonably certain, differentiation of the abundant osteoclasts can be attributed to an excess of parathormone, it is of interest to observe that large numbers of these cells could subsequently be sustained for sixteen weeks by

normal levels of parathormone (as indicated by the postoperative reversion to normal serum calcium levels). This is in conflict with such statements as that of Baker (quoted by Hancox[3]) to the effect that osteoclasts not only differentiate rapidly but also disappear quickly and the claim made by Weinmann and Sicher[8] that osteoclasts normally disappear after destruction of bone and that their persistence is attributable to the influence of excess parathormone.

Fig. 11.—Enlargement of section through the lesion on the right side showing extensive multifocal new bone formation, dark areas denoting vestiges of the lesion. (Hematoxylin and eosin stain. Magnification, ×12; reduced 5/7.)

Fate of Osteoclasts.—Controversial views have been expressed concerning the ultimate fate of osteoclasts. Several early authors adhered to the belief that osteoclasts could revert to osteoblasts or reticular cells. Hancox[2] showed experimentally that such reversion was unlikely. However, Heller and colleagues,[4]

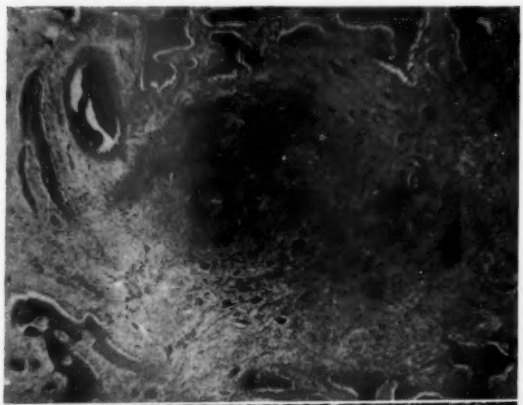

Fig. 12.

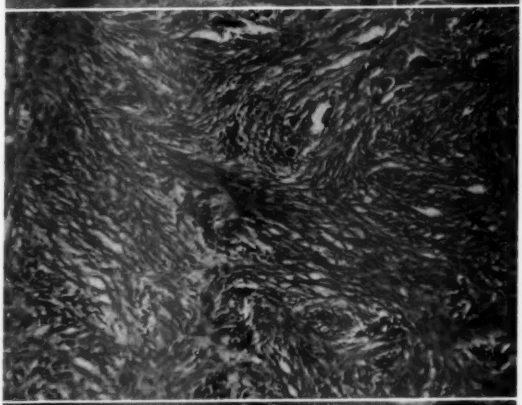

Fig. 13.

Fig. 14.

Fig. 12.—Focal accumulation of giant cells. New bone forming peripherally. (Solochrome cyanin stain [Pearse]. Magnification, ×35; reduced ⅝.)

Fig. 13.—An example of the realignment of fibers in an area from which giant cells have disappeared. (Hematoxylin and eosin stain. Magnification, ×150; reduced ⅝.)

Fig. 14.—High magnification of a typical area of active new bone formation. (Hematoxylin and eosin stain. Magnification ×750; reduced ⅝.)

in a study of egg-laying birds, observed that medullary bone is formed, resorbed, and formed again, all within a matter of hours. They contended that these extremely rapid reversals of function which they saw occurring daily in hens had been overlooked by Hancox and that the rapidity of change indicated a single identity of the cells responsible for formation, maintenance, and resorption of bone. All the slides examined in the present case support the view

Fig. 15.

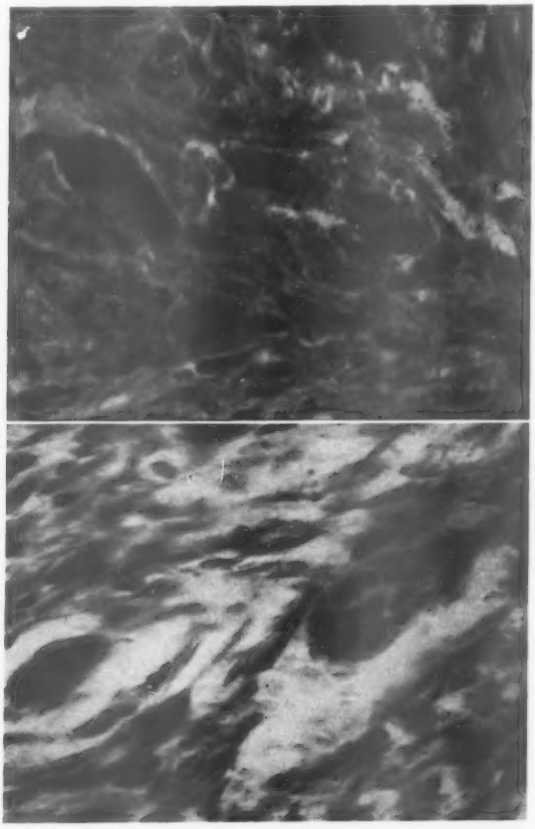

Fig. 16.

Fig. 15.—Tangential section of a small capillary in the lumen of which at least two giant cells can be seen. (Hematoxylin and eosin stain. Magnification, ×750; reduced ⅝.)

Fig. 16.—Transverse section showing osteoclast in lumen of capillary. (Hematoxylin and eosin stain. Magnification, ×600; reduced ⅝.)

of Hancox rather than that of Heller and associates. Far from any possibility of reversion, a clear-cut separation between osteoclasts and osteoblasts appears to exist, and the differentiation of osteoblasts is seen only in those areas most distant from the location of osteoclasts.

Hancox[3] reviewed two other possibilities in regard to the fate of osteoclasts. He thought it possible that some of these cells might undergo degeneration and succumb to local phagocytosis. Such osteoclasts are said to show intense eosinophilia, grossly vacuolated cytoplasm, and distorted, often pyknotic, nuclei. Several examples of cells approaching this description could be found, especially in sections from the left mandible. One is reluctant to draw distinctions at a cytologic level, however, when fine cellular detail may have been obscured by fixation and decalcification artifacts.

The final possibility put forward by Hancox is that the cells may find their way back into the circulation and thence to the spleen or lung. Several of the slides studied in this case lend support to this theory. In all cases the osteoclasts are aggregated in the areas of maximum vascularity, and in many instances they are observed in close relationship to small vessels (Figs. 15 and 16) which, as they proliferate, appear to assimilate the giant cells into the blood stream.

Clinical Considerations.—From the clinical viewpoint, certain points of interest emerge from a study of this case. Initial manifestations of hyperparathyroidism in the jaws are by no means uncommon, and the case history in this instance was substantially similar to another recorded previously.[1] Weinmann[6] examined the mandibles of patients who had suffered from chronic renal insufficiency and found ample evidence of bone changes due to hyperparathyroidism. He was led to the conclusion that areas of bone which are the site of greatest growth or resorptive activity are likely to be sites where any increase in parathyroid activity will become manifest. This theory is acceptable to those who have devoted attention to the microscopic examination of mandibular bone; even in the edentulous mouth this bone, probably in response to masticatory stresses, is maintained in a characteristically labile state.

Of the foci detected in Weinmann's study, the smallest could not be discerned by x-ray but were identified histologically. In the present case as well, certain limitations of x-ray diagnosis are exemplified. The stage of healing that had been reached at the time of death was, in fact, considerably in advance of that depicted on the x-ray film. Nevertheless, the earliest diagnoses of hyperparathyroidism are most likely to be achieved fortuitously by the careful observation of roentgenograms taken for reasons not necessarily incidental. Since dental x-ray examinations have become an everyday procedure, it is probable that the bone of the jaws comes under roentgenologic surveillance more regularly than any other part of the skeleton, so that the importance of recognizing early manifestations in the maxilla and mandible needs no emphasis.

Finally, in regard to the prognosis of bone lesions produced in hyperparathyroidism, this case indicates that the healing of large lesions is a lengthy process, involving extensive redeposition and remodelling of bone. McLean[5] probably errs on the side of optimism in stating that the removal of fibrous tissue and its replacement by normal bone take place rapidly. In the present case the swelling of the denture-bearing area was a source of discomfort, and surgical measures were under consideration shortly before the patient's death. In the light of the histopathologic studies, it would appear that surgical procedures in cases of this nature would be justified as a means toward assisting the gradual elimination of giant-cell foci and expediting the lengthy process of remodelling.

SUMMARY

The enlargement of mandibular lesions in a case of hyperparathyroidism is recorded, and their subsequent regression is traced until sixteen weeks postoperatively.

Necropsy material obtained at that stage provides the basis for a histologic study of the healing process. From this study evidence is adduced to indicate that the osteoclasts differentiated in abundance in the presence of excess parathormone are capable of survival after the return to normal parathormone levels, that their removal is probably effected by absorption into the circulation, that new bone cannot be formed in their immediate proximity, and that the conversion of osteoclasts to osteoblasts does not occur in this condition.

Healing appears to occur in two distinct phases: (1) segregation of osteoclasts, red cells, and debris to a central nidus and (2) peripheral encroachment by new bone formation.

The labile state of bone in the jaws is thought to favor the development in these sites of lesions related to parathormone excess. This lends importance to x-ray examinations of the jaws.

I am grateful for the help and encouragement that I have received from Sir Wilfred Fish, who first saw the patient, and Mr. A. Dickson Wright, F.R.C.S., who removed the parathyroid adenoma. I am obliged to Mr. E. B. Brain for the photomicrographs.

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ENDODONTICS

The American Association of Endodontists

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HISTOLOGIC EVALUATION OF PULP REACTIONS TO OPERATIVE PROCEDURES

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(Continued from the October issue, page 1248)

OBSERVATIONS AND DISCUSSION OF PULP REACTIONS TO DIRECT FILLING RESINS, SILICATE CEMENT, AND AMALGAM WITH AND WITHOUT LINERS

As it has been shown that odontoblast nuclei regularly enter the dentinal tubules in case of dry preparation,[10, 12] the present material was prepared under application of an ample water spray in order to avoid this reaction of the odontoblasts. There are a few exceptions to this rule, which will be indicated in the respective cases. It has been shown in the first part of this article (Oral Surg., Oral Med. & Oral Path. **12**: 1235-1248, 1959) and in a previous publication[12] that migration of the odontoblasts occurs when the dentine of the floor of the cavity is blown dry, even if the preparation has been carried out under a water spray. Accordingly, this procedure has been avoided in the present experiments. In this way, the reactions observed would originate exclusively from the effect caused by the filling material in question and a possible after effect of the cavity preparation.

As a typical example of pathologic reactions revealed after short observation periods, the effect caused by the direct filling resin, Texton, inserted into cavities lined with De Trey's cement should be described. A strong concentration of inflammatory cells had accumulated in the pulp tissues subjacent to the dentinal tubules involved (Fig. 1, *A*). Odontoblast nuclei were observed in the cut dentinal tubules and, because these odontoblasts deteriorate, neutrophilic leukocytes had accumulated in the odontoblast layer (Fig. 1, *B*). More centrally, the pulp tissue revealed numerous lymphocytes and transition

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forms of inflammatory cells (Fig. 1, *C*), and even a few neutrophilic leukocytes together with extravasated erythrocytes (Fig. 1, *D*). Some authors[24] do not consider the number of infiltrating inflammatory cells an important

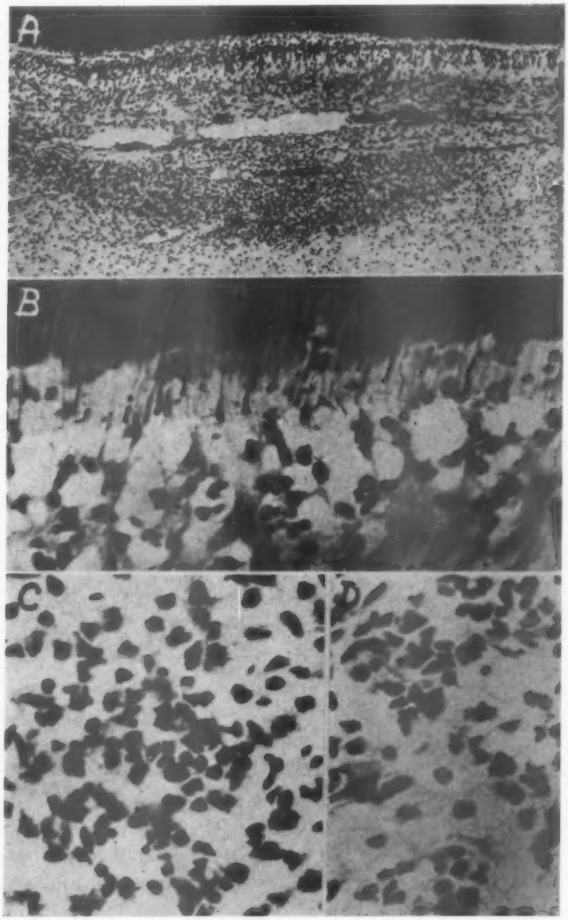

Fig. 1.—Cavity lined with De Trey's cement and filled with Texton. Observation period, two days. Cavity—pulp distance, 1.8 mm.

A, Pulp tissue subjacent to cavity, showing acute inflammation.

B, High magnification of area where the cut dentinal tubules end. Odontoblast nuclei in dentinal tubules. Neutrophilic leukocytes in disrupted odontoblast layer.

C, Lymphocytes and transition forms of inflammatory cells.

D, Neutrophilic leukocytes among scattered erythrocytes.

criterion of a pulp reaction. This is not in accordance with the view commonly expressed in textbooks of pathology, namely, that the general response of the organism to injury consists of accumulation of inflammatory cells and circulatory disturbances.

A typical example of an acute tissue reaction to injury will serve as our next basis for evaluation of pulp reactions observed after longer observation periods. A case will be described in which the direct filling resin, Sevriton,

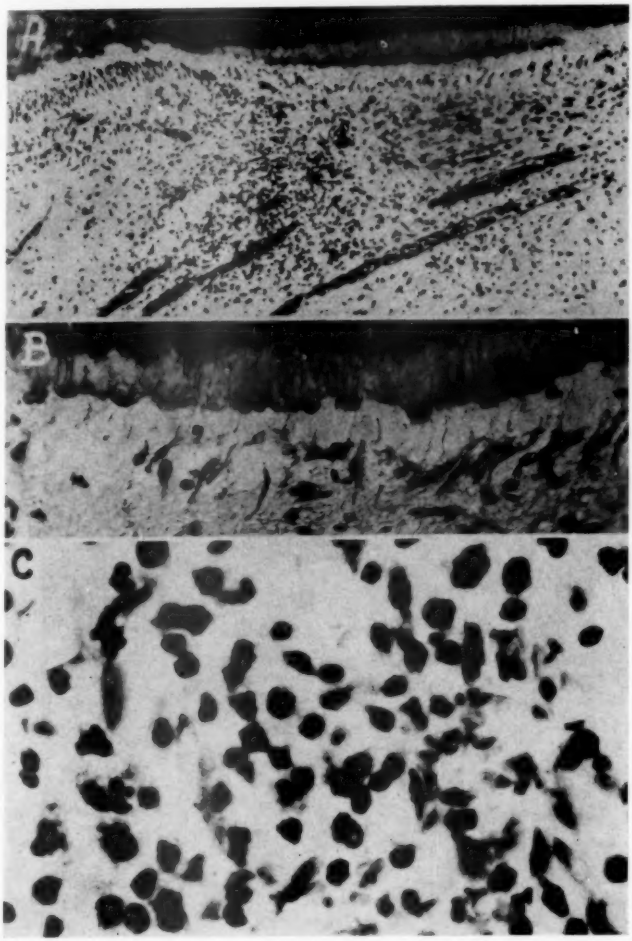

Fig. 2.—Cavity lined with S. S. White cement and filled with Sevriton. Observation period, 104 days. Cavity—pulp distance, 1.6 mm.

A, Pulp injury subjacent to cavity. Note irritation dentine, reduced odontoblast layer, accumulation of inflammatory cells centrally.

B, Irritation dentine containing fewer and more irregular dentinal tubules. Note that there has been no new formation of odontoblasts.

C, Lymphocytes, plasma cells, and macrophages indicating chronic inflammation. (Courtesy of B. Nygaard Östby.)

lined with S. S. White cement, had been left in the cavity for 104 days. Contrary to what was found in the experiments of short duration, no inflammatory cells were visible in the odontoblast layer near the predentine, and there were

no odontoblast nuclei in the dentinal tubules (Fig. 2, *A*). This is, however, a common observation in experiments of more than three or four weeks' duration. It is, nevertheless, evident that a reaction had taken place at the beginning of

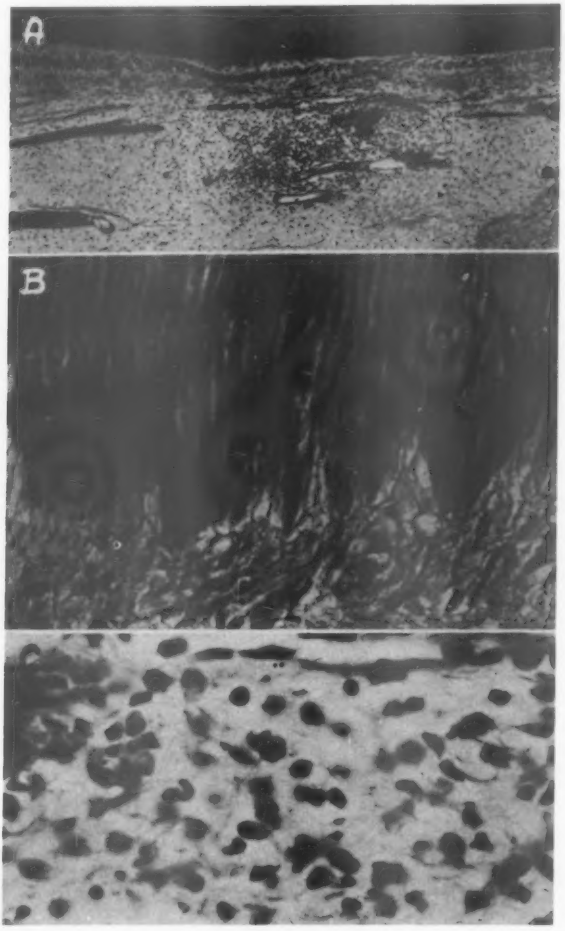

Fig. 3.—Cavity lined with De Trey's cement and filled with Orthofil. Observation period, 105 days. Cavity—pulp distance, 1.8 mm.

A, Pulp injury subjacent to cavity. Note irritation dentine, reduced odontoblast layer, accumulation of inflammatory cells, and disturbance in the circulation.

B, Section stained after the method of Masson, showing distinctly collagenous tissue. At top of *B*, note regular dentine lined by irritation dentine containing fewer and irregular dentinal tubules; this indicates deterioration of odontoblasts.

C, Lymphocytes, plasma cells, and machrophages indicating chronic inflammation.

the experiment. The odontoblast layer was markedly reduced and the irritation dentine contained fewer dentinal tubules than the adjacent dentine which was formed before the insertion of the filling (Fig. 2, *B*). Accordingly, the irritation dentine must be considered to be a scar tissue.

More centrally in the pulp tissue, in the area subjacent to the cut dentinal tubules, a concentration of cells was found. The cells were lymphocytes, plasma cells, and macrophages (Fig. 2, *C*), indicating a chronic inflammation.

When pathologic reactions have been observed and reported as a result of insertion of one filling material, manufacturers of other brands of the same kind of filling material sometimes will claim that their product never causes similar pathologic reactions. After application of various makes of direct filling resins in the present experimental series, no such variations in the effect of the inserted fillings could be observed. As an example, the reaction to the direct filling resin, Orthofil, should be mentioned. The cavity was lined with De Trey's cement, and the observation period was 105 days. Under the cavity corresponding to the cut dentinal tubules, an irritation dentine had been formed and the odontoblast layer appeared reduced. There were circulatory disturbances, including stasis, in some of the vessels of the area involved and, in addition, a strong concentration of inflammatory cells (Fig. 3, *A*). The irritation dentine, containing fewer and more irregular dentinal tubules than the surrounding dentine formed during the same period of time, must be interpreted as a clear evidence of deterioration of odontoblasts (Fig. 3, *B*). The lymphocytes, plasma cells, macrophages, and transition forms, mixed with extravasated erythrocytes, were evidence of a chronic inflammatory reaction (Fig. 3, *C*). Thus, as one could expect, the reactions to filling materials made of a similar substance are identical.

Some manufacturers have been able to produce liquid liners which, in laboratory experiments, prevent any penetration of the monomer. Thus, when the monomer is surrounded by a membrane made of a liner of this kind, Unifolan I, no polymerization will take place.[9] However, the pulp reactions to Texton were again similar to those described earlier, in cases in which Unifolan had been used as a liner strictly in accordance with the directions of the manufacturer. A reduced odontoblast layer bordered a zone of irritation dentine (Fig. 4, *A*). Contrary to what was seen in experiments involving similar observation periods, a little abscess was observed close to the predentine, and some neutrophilic leukocytes were seen in the loosely formed predentine (Fig. 4, *B*). This rather extraordinary reaction after such an observation period is related possibly to the depth of the cavity. More centrally, pulp cells of the chronic inflammatory type (Fig. 4, *C*) and an unusually large number of eosinophilic leukocytes (Fig. 4, *D*) were seen.

It may be of current interest to compare the reactions caused by the direct filling resins with the reactions caused by the material which they were intended to replace, namely, the filling porcelains or silicate cements. Shortly after they had been introduced on the market, these materials were found to produce inflammatory reactions in the pulp. Among the first European publications dealing with the tissue reaction to silicate cements were those by Palazzi,[23] Fasoli,[5] and the most comprehensive one by Hellner.[6] Nearly all later publications dealing with the problem[15, 17, 25, 27] corroborate the conclusions of these first publications. My own experimental series reveal similar reactions when

silicate cements have been inserted without a liner and left in the cavity for 117 days. An irritation dentine, bordered by a reduced odontoblast layer, had formed while inflammatory cells had accumulated in the subjacent central part of the pulp (Fig. 5, *A*). Capillaries were clearly visible in the reduced odontoblast layer (Fig. 5, *B*), and the inflammatory cells were those usually seen in chronic inflammation of the pulp (Fig. 5, *C*). Generally it may be said that the reaction to unlined silicate cements is similar to the reaction caused by lined direct filling resins.

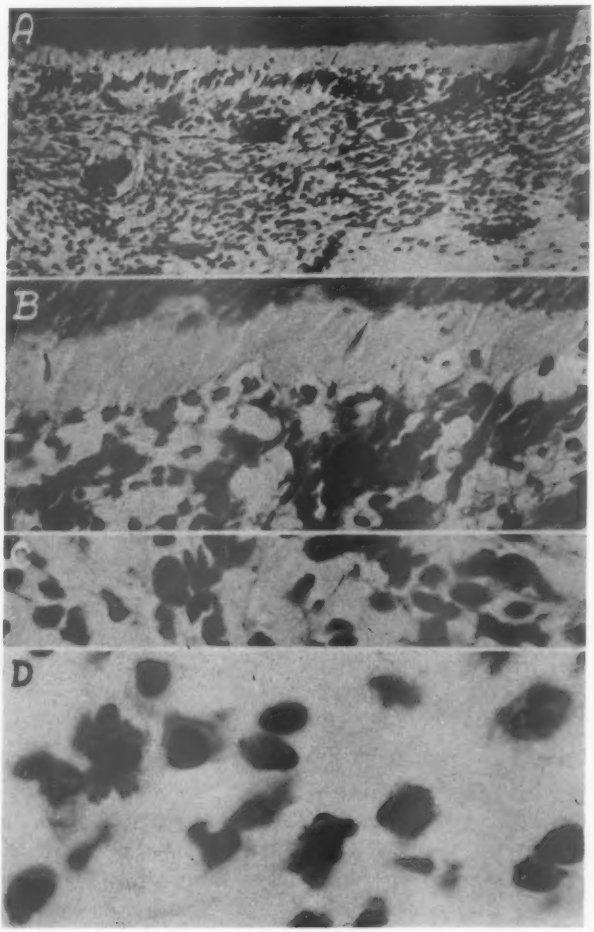

Fig. 4.—Cavity lined with Unifolan and filled with Texton. Observation period, ninety-eight days. Cavity—pulp distance, 0.6 mm.

A, Irritation dentine, neutrophilic leukocytes concentrated along predentine, disturbance of circulation, and accumulation of inflammatory cells centrally.

B, Inclusion of cells in irregular, loosely formed irritation predentine. Neutrophilic leukocytes in disrupted odontoblast layer.

C, Lymphocytes and macrophages located more centrally in the pulp. Note plasma cells and an unusual number of eosinophilic leukocytes.

The next problem will consist of observing whether the liners available will protect the pulp against the harmful effect of the silicate cements. When Kloroperka N-Ø, which really is not made for this purpose, was used experimentally, none of these reactions were observed (Fig. 5, *D*). The experimental tooth was a premolar of the same person as in the former case, and the observation period was identical. Similar conditions were observed when a thin layer of zinc oxyphosphate cement was used as a liner. A reduced inflammatory reaction was observed in cases in which Chembar and Pulpdent had been used

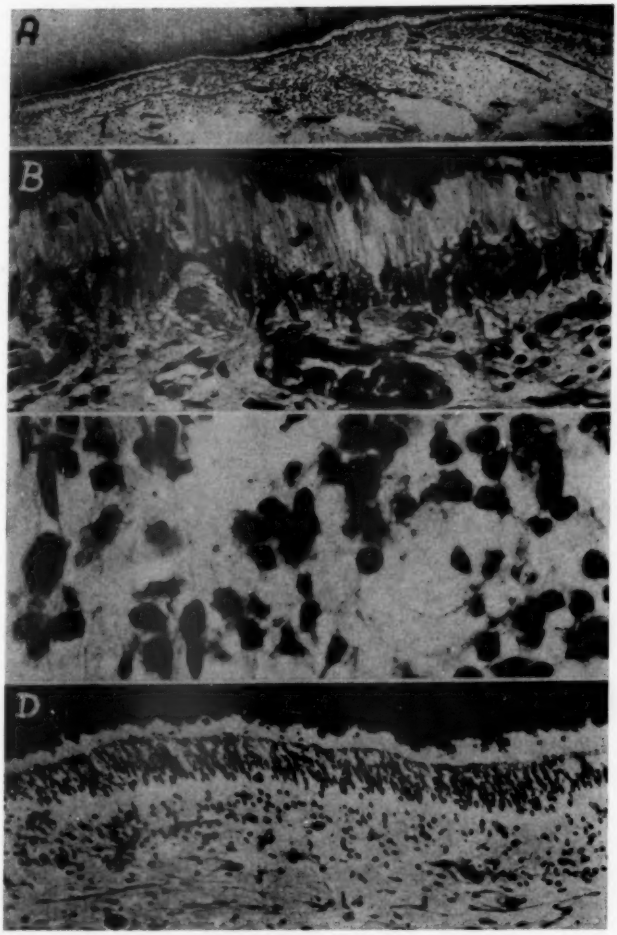

Fig. 5.—*A*, *B*, and *C*, Cavity filled with the silicate cement Syntrex. Observation period, 117 days. Cavity—pulp distance, 1.6 mm.

A, Irritation dentine, reduced odontoblast layer, accumulation of round cells.

B, Irregular predentine, reduced odontoblast layer, and hyperemia.

C, Lymphocytes and macrophages, to the left a macrophage containing cell remnants. Chronic inflammatory reaction.

D, Contralateral tooth from same person. Cavity lined with Kloroperka N-Ø and filled with Syntrex. No reaction.

as liners, but there was no full protection under such conditions.[28] Thus, unlike the direct filling resins, a zinc oxyphosphate cement will effectively protect the pulp against the harmful effect of the silicate cements.

The manufacturers of a new type of silicate cements, in which ceramic fibers constitute a part of the powder component, have claimed that this material is less irritating than ordinary silicate cements. As an example, the reaction caused by the material, Achatite, should be mentioned. Achatite had been left

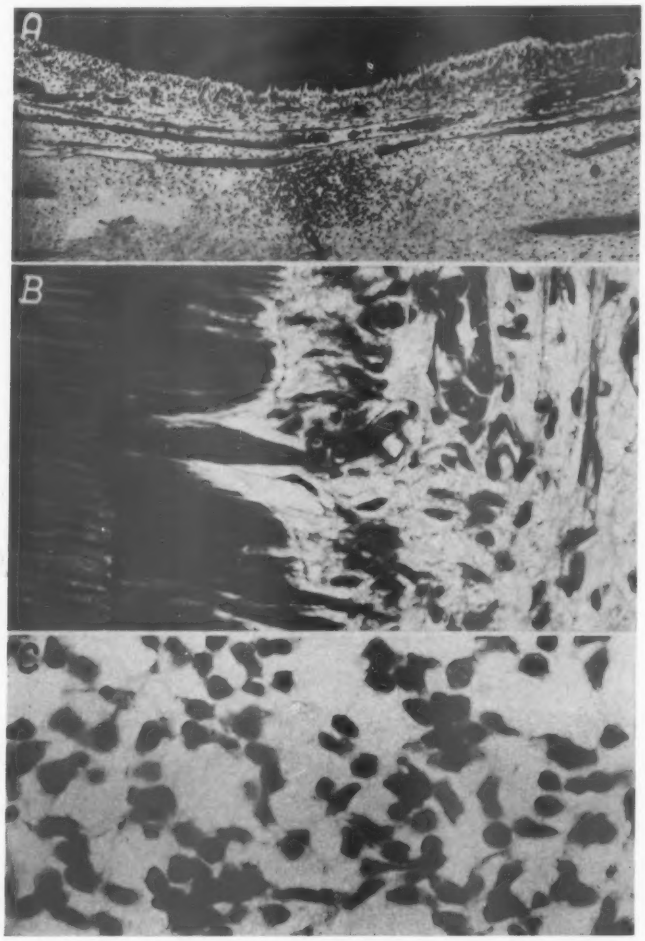

Fig. 6.—Cavity filled with the silicate cement, Achatite. Observation period, forty-four days. Cavity—pulp distance, 1.2 mm. Section stained by the iron hematoxylin method.

A, Irritation dentine, disturbance of circulation, accumulation of round cells.

B, Border of regular dentinal tubules indicating start of experiment, at which time odontoblasts migrated into their dentinal tubules. The reduced number of odontoblasts produced a reduced number of dentinal tubules, resulting in irregularity of the irritation dentine.

C, Lymphocytes and plasma cells indicating chronic inflammation.

in an experimental cavity for 44 days. Irritation dentine had formed, the odontoblast layer was reduced, there was a strong hyperemia, and inflammatory cells had accumulated (Fig. 6, *A*). Here it is clearly demonstrated that the

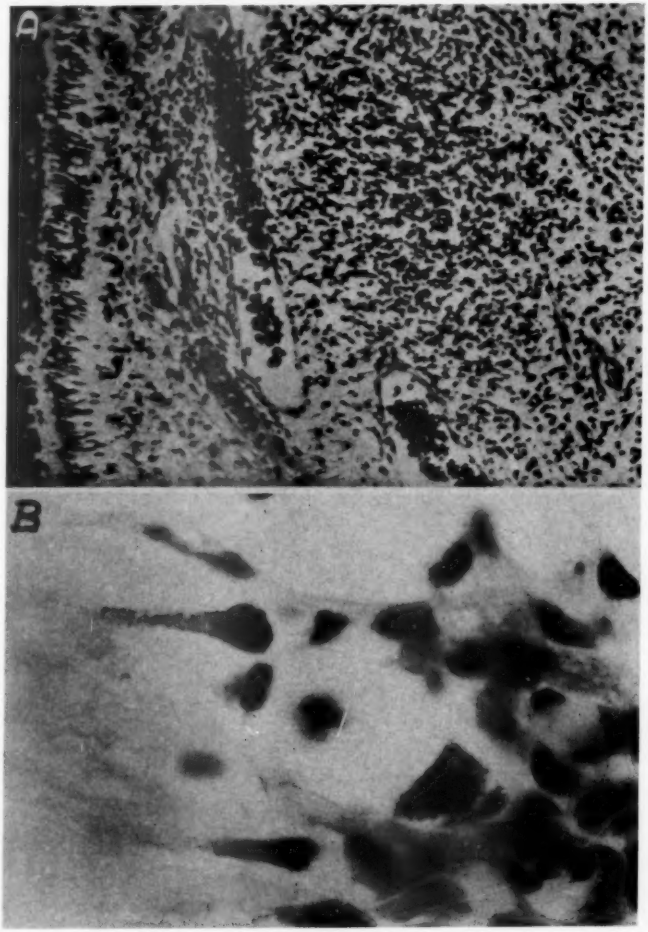

Fig. 7.—Cavity filled with the silicate cement, Achatite. Observation period, ninety-eight days. Cavity—pulp distance, 1.1 mm.

A, Severe inflammatory reaction.

B, Eosinophilic leukocytes with their cell bodies partly migrated into the loosely formed predentine.

dentinal tubules are running uninterruptedly in the primary dentine formed previous to the experiment. Reaching the border of the irritation dentine, some of them are discontinued; hence, the irritation dentine contains fewer dentinal tubules. Capillaries which penetrate the odontoblast layer are in contact with the predentine (Fig. 6, *B*). The inflammatory cells were mostly

lymphocytes and transition forms of inflammatory cells (Fig. 6, *C*). In a similar experiment with a somewhat longer observation period, comparable with cases in which silicate cements had been used, the reaction was severe (Fig. 7, *A*). In the loosely formed predentine subjacent to the cavity, eosinophilic

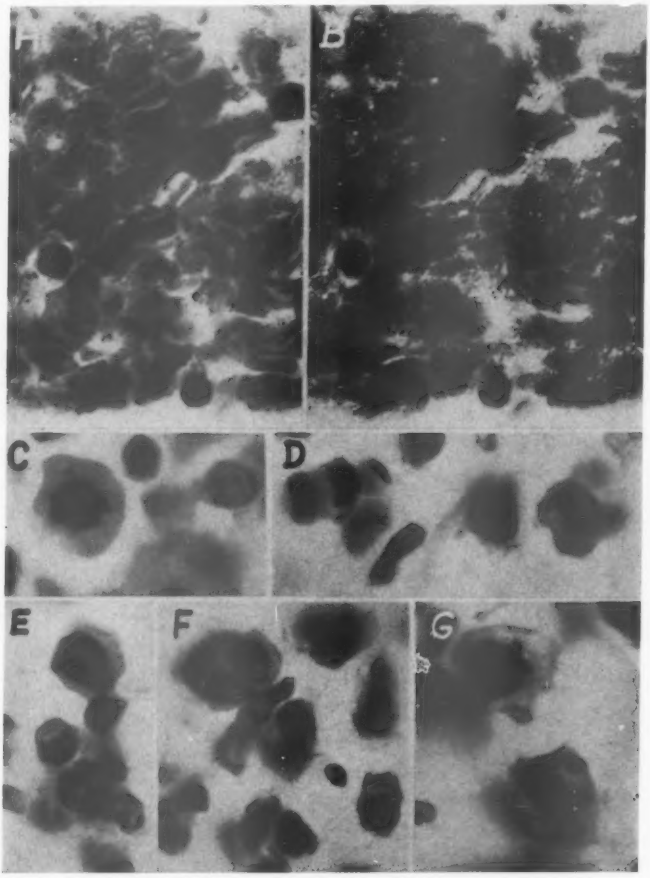

Fig. 8.—High magnifications of details shown in Fig. 7.

A, Brown pigment diffusely spread over section.

B, Same area in polarized light. Brown pigment birefringent, indicating deterioration of erythrocytes in vivo.

C and *D*, Mitoses in inflammatory cells.

E and *F*, Lymphocytes, plasma cells, and macrophages.

G, Deteriorating inflammatory cells. Chronic inflammatory reaction including stasis and hemorrhage.

leukocytes with their cell bodies partly in the dentinal tubules were observed, together with neutrophilic leukocytes and extravasated erythrocytes in the heavily deformed odontoblast layer (Fig. 7, *B*). Deterioration of erythrocytes

was evidenced by the presence of a brown pigment (Fig. 8, *A*), which in polarized light was shown to be birefringent. Among the inflammatory cells located in the pulp tissue, mitoses were observed (Fig. 8, *C* and *D*). The inflammatory

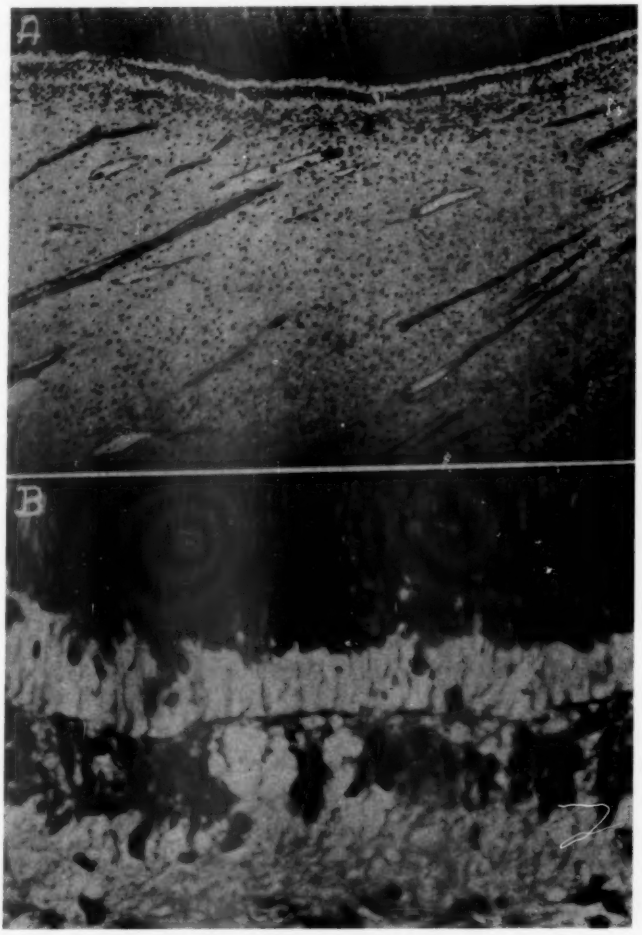

Fig. 9.—Another tooth from the same person as that shown in Fig. 2. Cavity filled with amalgam. Observation period, 104 days. Cavity—pulp distance, 1.7 mm. Careful drilling with Ritter engine, without water spray.

A, Narrow area of irritation dentine, no accumulation of cells.

B, Irritated dentine containing fewer and more irregular dentinal tubules, indicating loss of odontoblasts, 104 days after the insertion of the inert filling material, amalgam. Only the scar tissue is evidence of an acute reaction which has subsided. (Courtesy of B. Nygaard Östby.)

cells were those regularly seen in the chronic inflammation of the pulp tissue (Fig. 8, *E—G*). The conclusion here will be that an alteration of the powder components of the silicate cement, as previously described, does not

reduce the harmful effect of the silicate cement. On the other hand, the pulp may be protected by applying a thin layer of zinc oxyphosphate cement.

Finally, the pulp reaction to amalgam inserted without a liner should be described. The experimental tooth belonged to the same person as the one shown in Fig. 2, and the observation period was identical. No inflammatory cells could be observed after insertion of amalgam fillings under these conditions (Fig. 9, *A*). In some sections, however, interruption of the odontoblast layer could be observed in one area, peripheral to which the irritation dentine contained fewer dentinal tubules (Fig. 9, *B*), which indicates that in this case odontoblasts have deteriorated as an acute reaction to the filling procedure. This finding can be explained by the fact that this experiment was among my first, carried out at a time when the initial reactions to cavity preparation per se were not known. It is now known that odontoblast nuclei enter the dentinal tubules in spite of careful cavity preparation so long as water is not applied. It is also known that the migrated odontoblasts deteriorate, resulting in an acute inflammatory reaction in the adjacent odontoblast layer. This case therefore, is an example in which the acute inflammatory reaction has subsided after insertion of an inert filling material; a scar tissue has formed without causing a chronic inflammatory reaction in the pulp.

CLINICAL IMPLICATIONS

On the basis of the result of the present histologic investigation, the following clinical conclusions should be drawn:

(1) The patient should be summoned regularly for dental examination and treatment.

(2) X-ray and clinical examination should be carried out so that cavities may be found when they are superficial, before severe pulp involvements occur.

(3) The cavity preparations should be carefully performed. This includes the application of a sufficient water spray. Desiccation of the dentine and the enamel should be avoided.

(4) Careful washing with water and only superficial drying with sterile cotton should take place before the restoration is placed into the cavity.

(5) The entire area of soft dentine in all cavities should be removed. In cases of deep caries where no exposure of the pulp occurs, zinc oxide and eugenol should be used as an underfilling.

(6) In cases of perforation, endodontic treatment should be carried out according to modern principles, based on histologic investigations.

(7) Afterward the teeth should be restored, preferably with nonirritating filling materials. An adequate liner must be used where irritating materials (for example, silicate cements) are employed.

(8) The physical properties of the materials should be in accordance with the specifications of the American Dental Association's Bureau of Standards.

Following these rules, pulp involvements incident to operative procedures will be reduced and minimized.

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DISCUSSION OF DR. LANGELAND'S PAPER BY MAURY MASSLER

With each new paper, it becomes more apparent that dental science is just *beginning* to understand the biology of the pulp and has not yet achieved full appreciation of this curious and specialized connective tissue. This should suggest caution to every investigator, lest the conclusions which seem so valid today come back to haunt him ten years hence—as they haunt those who twenty years ago stated categorically and with finality: "An inflamed pulp is a dead pulp!" and "A painful pulp must die!"

The emphasis which Dr. Langeland has placed on the need for more accurate control in histologic evaluation of the effects of the operative procedures on the pulp is very well taken. Artifacts caused by inadequate fixation and staining are very common. The literature is therefore cluttered with long descriptions of what have turned out to be artifacts or, more politely, "uncontrolled observations." A good deal of work remains to be done in the techniques of fixation, cutting, and proper staining of the pulp—preferably with specific histochemical stains. To this I would further add the use of radiographic shadowgrams. There are various types of reparative dentine, ranging from regular, tubular dentine associated histologically with a normal healthy pulp to irregular, calcific scar tissue usually found associated with inflamed and often degenerating pulp tissue. These can be seen histologically but not roentgenographically. The roentgenogram can be misleading.

Fortunately, the effects of cavity preparation (and filling materials) are usually circumscribed to the area under the cut tubules, so that the adjacent or opposite areas can serve as "internal controls." This fact has been a real help to every investigator.

Dr. Langeland points out that the clinical criterion of pain is not a valid index to the histologic appearance of the pulp. To this I would add the electric pulp tester. Every investigator has had the experience of finding a wonderfully intact pulp under a lesion which has caused severe and chronic pain over many months. I am still surprised to find a fibrotic and degenerated pulp in a human specimen when there was no history of pain. It is apparent that we must soon do more than *talk* about the pain receptors in the pulp; we must do some serious studies in this direction. Are the odontoblasts the pain receptor cells in fact as well as in theory? If so, by which chemical mechanism is the pain triggered off? By histamine released by the injured cell, or by acetylcholine?

In discussing the paper with Dr. Langeland, I was pleased to hear him say that he, too, has seen youthful pulps in patients aged 70 years and that he is also dismayed by sometimes finding an old fibrotic pulp in a young patient. Drs. Marvin B. Weiss and Hilton Mello are examining the possibility that pulpal fibrosis and degeneration may follow from periodontal disease. The association seems to be more than accidental. If this proves to be correct, we shall have to re-examine the vascularity of the periapical tissue and its relationship to the nutrition of the pulp.

Many experiments by many different laboratories need to be completed before the whole story of pulpal reactions can be told. It is much too early for absolute conclusions.

I should like to raise a disturbing thought as this time. We have noted that the pulpal cells and capillaries immediately under the sharp corner of a cavity preparation often show more severe damage than the area under the center of the same cavity preparation. When a hand instrument was used to sharpen that line angle, the damage to the pulp seemed to be more severe than when a bur was used. It might be instructive to study and to compare the effects of hand instrumentation on the pulp. I am confident that if we do this, we shall find something factual to replace the current unsupported cliché that hand instruments are not harmful to the pulp. In fact, I am persuaded that in children, and in my own teeth, hand instrumentation is more painful and less tolerable than a fast-cutting, smooth-running, well-lubricated bur.

If one is looking for conclusions, however, perhaps the most striking conclusion that one can draw at this time (and one which Dr. Langeland brings out very well) concerns the *relative* amount of pulpal damage which can be caused by operative procedures, medicaments, desiccants, and filling materials. The most severe damage observed under a deep cavity cut by a "hot" bur is still much less than that caused by a single application of

silver nitrate solution or by a silicate filling placed without a liner. Even a phosphoric acid cement used in bulk as a filling causes more damage than a bur cutting at 30,000 r.p.m. without a water collant. Although dentine is a fairly good heat insulator, it is notoriously susceptible to damage by acid. Fortunately, it recovers very well from acute trauma, *once the insult is removed.* But, as Dr. Langeland shows, it succumbs when the irritant is continuous, as under a silicate or acrylic filling.

It is refreshing to hear Dr. Langeland refer to the work of other investigators. Apparently he reads the literature and learns not only from his own experience. This is a virtue that all investigators should cultivate. It is sad to read papers which describe anew procedures and experiments and findings reported twenty and thirty years ago in other countries. Earlier today I listened to papers which reported, as if they were new and original, findings published in the Swiss and German literature twenty and thirty years ago.

We have come a long way toward the appreciation of pulpal biology, but there is still a long road to travel before we can reach understanding. We need many more dedicated and careful workers like Dr. Langeland to build this road for us. Dedication and sincerity, however, are not enough. The investigator must have scientific training in the proper use of scientific tools in addition to his enthusiasm if the truth is to be found. Dr. Langeland meets all these requirements.

RESEARCH

THE EFFECT OF VITAMIN A DEFICIENCY ON THE PERIODONTAL STRUCTURES OF RAT MOLARS, WITH EMPHASIS ON CEMENTUM RESORPTION*

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INTRODUCTION

VITAMIN A deficiency as it affects the periodontium has been studied by various investigators,[1-6] and there are differences of opinion regarding its effect on the periodontal structures, particularly cementum. This study was undertaken in an endeavor to broaden the knowledge in this field and to answer the following questions: (1) What is the effect of vitamin A deficiency on the periodontal structure in general and on the cementum in particular? (2) Does vitamin A deficiency enhance cementum resorption, and to what extent? (3) Is there any difference because of sex, surface, and tooth involvement?

MATERIALS AND METHODS

Eighteen male and twenty-seven female albino rats, each 40 days old and weighing 60 to 110 grams, were used for this study. A ready mixed vitamin A-deficient diet (Diet I) was used. The composition of the diet used is as follows:

Vitamin A Test Diet U.S.P. (Diet I)†

Composition:	
USP salt mixture #2	4 per cent
Irradiated yeast (vitamin D)	8 per cent
Starch	65 per cent
Vegetable oil	5 per cent
Vitamin A test casein	18 per cent

From the M. D. Anderson Hospital and University of Texas Dental Branch.
Presented at International Association for Dental Research (Minnesota Section) meeting in the spring of 1956.
*This work was done at the School of Dentistry, University of Minnesota, Department of Periodontology, as requirment for Master Thesis.
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†Vitamin A-deficient diet and vitamin A concentrate were obtained from Nutritional Biochemical Corporation, Cleveland 28, Ohio.

Salt Mixture #2

Composition:

Calcium biphosphate	13.58 per cent
Calcium lactate	32.70 per cent
Ferric citrate	2.97 per cent
Magnesium sulfate	13.70 per cent
Potassium phosphate (dibasic)	23.98 per cent
Sodium biphosphate	9.72 per cent
Sodium chloride	4.35 per cent

In order to avoid any discrepancy in the experiment as to difference in the hardness and roughage in the diets fed to the control and experimental animals, the same vitamin A-deficient diet was used for the control animals with the addition of 4.5 grams of vitamin A concentrate* (200,000 i.u.) per gram per 100 pounds of diet. Both Diets I and II met the daily requirement except for the addition of vitamin A to Diet II.

The rats were housed in a temperature- and light-controlled room in wire cages which were kept and arranged so that daily cleaning was possible without much disturbance to the animals. Thirty of the animals (eighteen females and twelve males) were fed on Diet I "experimental," and the other fifteen (nine females and six males) were on Diet II "controls." Each animal was provided with food and water ad libitum. The experiment was conducted for thirteen weeks, at the end of which time the rats on Diet I showed signs of vitamin A deficiency. The changes observed were eye changes (xerophthalmia and keratomalacia), irregular whirling of the incisors, dryness of the skin, loss of weight, and cessation of growth. Some of the experimental animals died during the ninth and tenth weeks of the experimental period. During the experimental period one control animal and ten animals from the experimental group (seven females and three males) died.

At the end of the thirteen-week period, the animals were sacrificed and the jaws, femur, internal organs (liver, spleen, kidney, parotid gland, submaxillary gland, heart, lungs, and skin) were removed. The jaws were fixed in Zenker's solution and the soft tissues in 10 per cent formalin. The jaws were decalcified in 5 per cent nitric acid and embedded in celloidin, and the soft tissues were embedded in paraffin. Histologic sections 12 microns thick were cut midsagitally through the three molar teeth of the lower right quadrant. Soft-tissue sections were cut in 6 micron thicknesses. All sections were stained with hematoxylin and eosin. A minimum of five jaw sections were mounted with Clearite on standard microscopic slides.

All jaw sections were examined for histologic change in the periodontal structures. Soft tissues were studied histologically to establish that we were dealing with a vitamin A deficiency state in the experimental animals.

Concentrated study was made of the areas of cementum resorption. The method employed to determine the areas of cementum resorption was the same as that used by Henry and Weinman[7] in their study on human cementum.

*Vitamin A-deficient diet and vitamin A concentrate were obtained from Nutritional Biochemical Corporation, Cleveland 28, Ohio.

The length of the resorption areas was determined by measuring the greatest diameter between the deepest point of penetration and a plane that corresponded to the reconstructed surface of the root. The following method was devised to measure the area of resorption:

With a microprojector, the jaw sections were projected at a magnification of ×150 on a hard cardboard fixed on the wall. The outline of the root portion of the tooth was drawn on a sheet of white paper fixed to the cardboard. The root portion was shaded with lead pencil, whereas the areas of cementum resorption were shaded with red. The root length of each surface of the tooth and the areas of cementum resorption were determined by means of dividers. The same sections were further checked for verification by going back to the microscope and measuring the areas with an eyepiece micrometer in units which were later converted into millimeters. Of course, the depth was always measured with the eyepiece micrometer.

The type of cementum resorption and repair was also studied. For purposes of description and convenience, these were classified into three types (active, reparative, and aplastic), as described by Henry and Weinman.[7]

In order to determine whether there was any difference in the amount of cementum resorption in the two groups, the data were carefully assembled in tables according to surface, areas measured, and area involved in cementum resorption for purposes of comparison; a ratio was computed from the amount of cementum resorption and the total root length. The difference between percentages was divided by the standard error of the difference between percentages, and the relative deviate thus found was referred to the normal probability table to establish whether or not the percentage difference was statistically significant at the 0.05 level of confidence.

The following formula was applied:

$$x = \frac{P_1 - P_2}{SE_{p_1 - p_2}} = \frac{P_1 - P_2}{\sqrt{P_{q\frac{(n_1 + n_2}{n_1 \times n_2)}}}}$$

Where $P = \frac{f_1 \; f_2}{n_1 \; n_2}$

and f_1 and f_2 are the numbers for experimental and control groups, respectively, that exceeded the mean and n_1 and n_2 being the numbers of the sections studied in the experimental and control groups

and $q = 1 - P$

A value of $n = > 1.96$ is of statistical significance at the 0.05 level of confidence, and a value of $n = 3.30$ is of statistical significance at the 0.001 level of confidence.

To show differences in the amount of cementum resorption in different teeth, figures of total root lengths and the amount of cementum resorption for a single tooth on all three surfaces (mesial, distal, and bifurcation) were combined and the percentage was computed to compare the experimental group with the control group.

Root length and root resorption on the same surface (mesial, distal, and bifurcation) of the three molar teeth were combined. Percentages were computed to compare the experimental group with the control group to show any difference due to surface involvement. Separate tables were made for the males and females of both groups to show whether sex had any influence on cementum resorption.

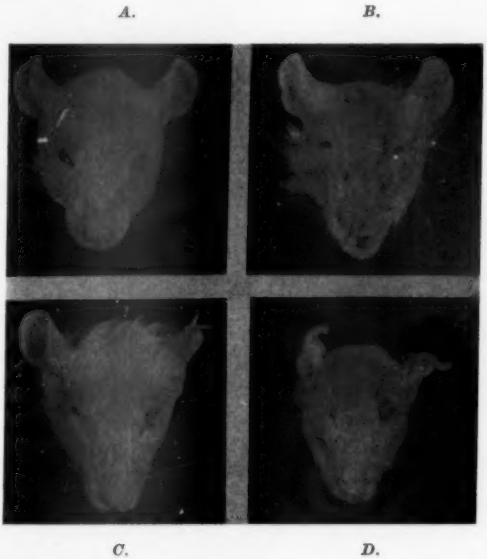

Fig. 1.—Eye changes due to vitamin A deficiency. *A*, Normal eye. *B*, Note puffiness around the eyes which denotes that ophthalmia is about to appear. *C*, Edema and ulceration of the eyelid are evident. *D*, Note marked edema and ulceration and complete blindness.

FINDINGS

The experimental animals lost weight and showed muscular weakness and humped posture. The fur was rough, and typical eye signs (keratomalacia and xerophthalmia) of vitamin A deficiency were noticed (Fig. 1). The following changes in the soft tissues due to vitamin A deficiency were noticed:

A. *Spleen (Fig. 2):* The spleen stained less red than the normal, and fairly large amount of hemosiderin pigment was seen. There was a marked increase in the size of the lymphoid follicle at the expense of the polypoid tissue. There was a thickening of the walls of the blood vessels and of the capsule.

B. *Testes:* The lining of the seminiferous tubules was disorganized; the cell lining lost its normal pattern. The cells showed marked edema.

C. *Liver and adrenal gland:* No changes were seen.

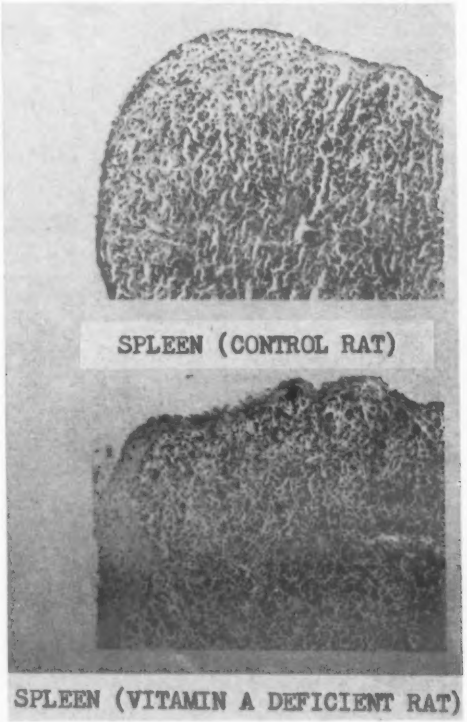

Fig. 2.—Spleen. Note excessive hemosiderin pigment and thickening of the capsule.

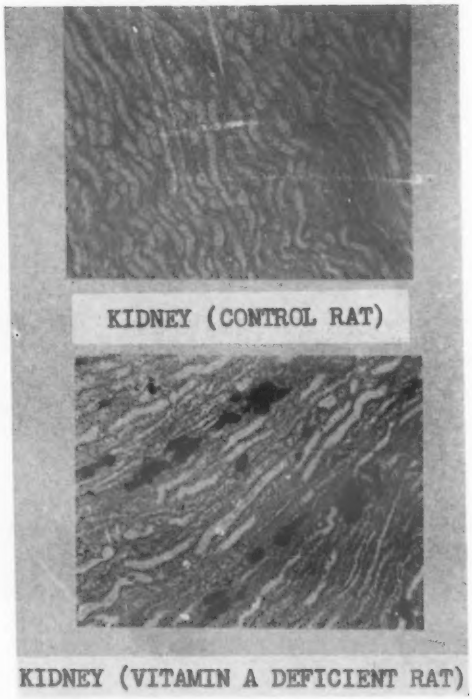

Fig. 3.—Kidney. Note calcification of urinary tubules.

D. *Heart muscle:* Slight myocarditis was seen.

E. *Parotid and submaxillary glands:* Marked atrophy and edema with complete absence of infection or cellular infiltration were evident.

F. *Lung:* There was dilation of some of the alveolar spaces. The majority of them were occluded by fluid. There was complete absence of infection or cellular infiltration.

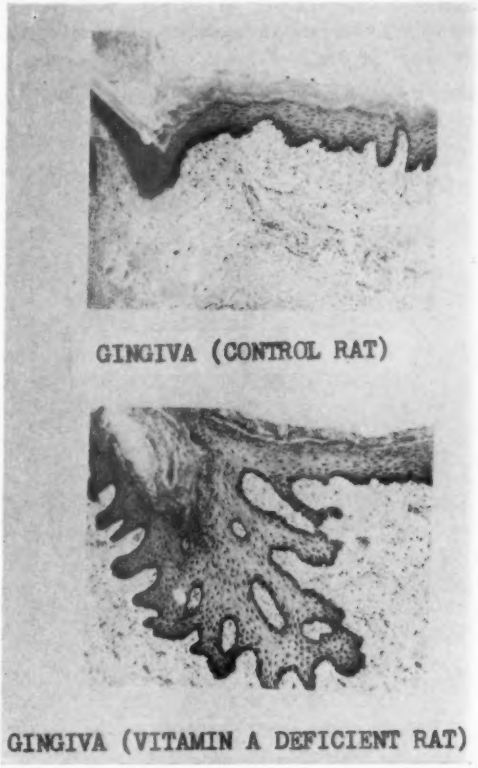

Fig. 4.—Gingiva. Note hyperplasia and hyperkeratosis.

G. *Skin:* The epidermis showed marked keratinization (hyperkeratosis). Connective tissues did not show any change; slight but demonstrable atrophy of the sebaceous gland of the hair follicle was seen.

H. *Kidney (Fig. 3):* There was deposition of the calcium salts* (urinary calculi) in both the cortex and the medulla. Areas of patchy interstitial nephritis were seen. The urinary tubules were dilated.

*Calcium salts in the kidney were demonstrated by special von Kossa silver stain.

CHANGES IN THE PERIODONTAL STRUCTURES:

1. *Gingiva (Fig. 4) and Epithelial Attachment.*—In the gingiva the area studied was the papilla on the mesial aspect of the first molar, and the characteristic changes noticed histologically were hyperkeratinization (hyperkeratosis) and hyperplasia. The hyperplasia was seen both in an increase in the number of epithelial cells and in the projection of fingerlike processes into the subjacent connective tissue. No downgrowth of epithelial attachment was noticed. There was no evidence of cellular or leukocytic infiltration in either the control or the experimental group. Connective tissue fibers showed no change.

2. *Alveolar Bone (Fig. 5).*—Normal architecture of alveolar bone was disturbed. There was increased osteoclastic activity and very little remodeling or building of bone (osteoblastic activity).

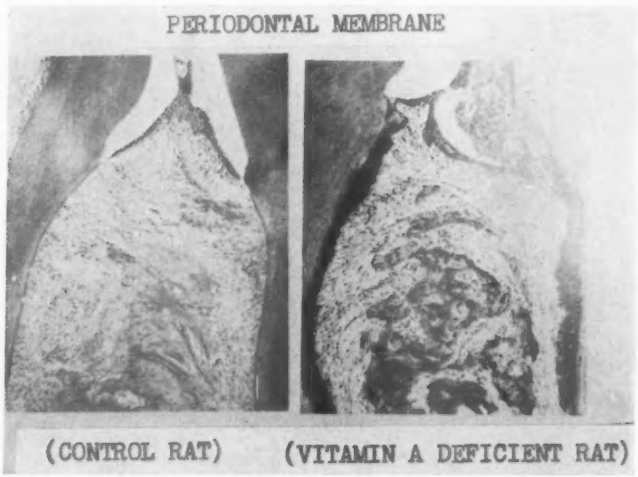

Fig. 5.—Periodontal membrane. Note irregular narrowing and calcification of periodontal fibers.

3. *Periodontal Membrane (Figs. 5 and 6).*—The periodontal membrane space was irregularly narrowed. There was calcification of the periodontal fibers, starting from the cementum side of the tooth. This was especially prominent near the cementoenamel junction.

4. *Cementum (Fig. 6).*—There seems to be more cementum resorption in the vitamin A-deficient animals than in the control animals (Tables I, VI, and IX). In the areas of cementum resorption there is reparative activity by a bonelike material, resulting in ankylosis of teeth.

The statistical analysis of Table I is assembled in Table IX. From this, it is apparent that there is significantly more cementum resorption in the

groups of rats on the vitamin A-deficient diet. This conclusion did not hold true for all surfaces (Tables I, III, and IX). The cementum resorption on the mesial and bifurcation surfaces is significantly increased (to the 0.05 level of confidence), while the cementum resorption on the distal surface was not significantly different between the two groups.

It was interesting to note the tremendous differences of cementum resorption on different surfaces (Table III). In relation to the root length, the greatest amount of resorption always occurred in the bifurcation area. This held true for both the experimental and the control groups. In the control group the mesial surface had the least amount of resorption, while the experimental group had the least amount of resorption on the distal surface.

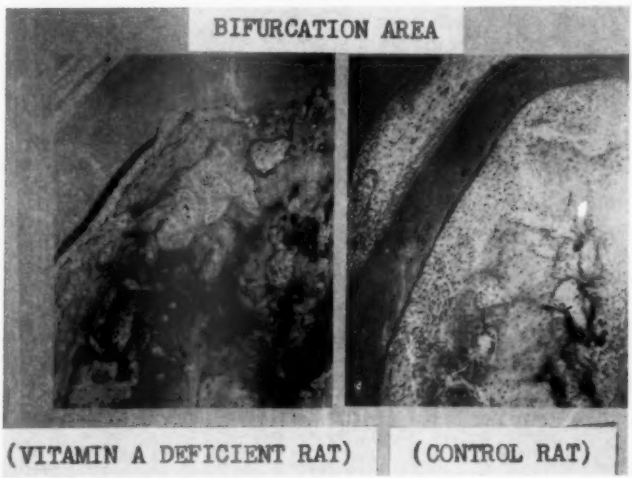

Fig. 6.—Cementum. Alveolar bone atrophy, cementum resorption, narrowing of periodontal space, and ankylosis of tooth are shown.

In order to study the question of whether tooth resorption was equally great on all three molars the relevant data were assembled in Table V. It can be seen that the first molar shows maximum cementum resorption and third molar the least resorption in both the experimental and the control groups.

Finally, we were interested in finding out whether sex had anything to do with the amount of cementum resorption. This may be answered by studying Tables II, IV, and VI. Table II shows the amounts and relative percentages of cementum resorption in both male and female animals of the experimental and control groups. Whereas Tables IV and VI show the results of cementum resorption as related to surface and tooth involvement, it is apparent that cementum resorption occurred in male and female animals of both groups. Findings and distribution of cementum resorption according

TABLE I. RELATION OF RESORPTION AREA IN CEMENTUM TO ROOT LENGTH

SURFACE		TOOTH: THIRD MOLAR — AREA OF RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT	SECOND MOLAR — AREA OF RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT	FIRST MOLAR — AREA OF RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT
Distal	C	0.760	0.056	7.4	0.041	5.39	0.890	0.166	18.65	0.029	3.25	1.004	0.051	5.08	0.016	1.59
	E	0.786	0.061	7.76	0.0193	2.41	0.878	0.120	13.66	0.022	2.50	0.841	0.053	6.30	0.011	1.30
Mesial	C	0.921	0.060	6.51	0.005	0.54	0.714	0.024	3.36	0.002	0.28	1.166	0.128	10.98	0.013	1.11
	E	0.748	0.159	21.25	0.010	1.33	0.783	0.057	7.27	0.004	0.51	0.976	0.177	18.13	0.016	1.63
Bifurcation	C	1.203	0.129	10.72	0.008	0.66	1.345	0.222	16.50	0.006	0.44	2.086	0.452	21.67	0.023	1.10
	E	1.23	0.326	26.50	0.010	0.81	1.434	0.464	32.35	0.017	1.18	2.102	0.787	37.44	0.028	1.13

RL = Root length.
L = Length.
D = Depth.
C = Control.
E = Experimental.

TABLE II. SEX DISTRIBUTION OF DATA FROM TABLE I

SURFACE		TOOTH: THIRD MOLAR — AREA OF CEMENTUM RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT	SECOND MOLAR — AREA OF CEMENTUM RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT	FIRST MOLAR — AREA OF CEMENTUM RESORPTION: RL (MM.)	L (MM.)	PER CENT	D (MM.)	PER CENT
Distal	CM	0.776	0.044	5.67	0.013	1.67	0.876	0.166	18.94	0.031	3.53	1.054	0.088	8.34	0.024	2.27
	CF	0.765	0.064	8.36	0.058	7.58	0.899	0.166	18.46	0.028	3.11	0.975	0.029	2.97	0.010	1.0
	EM	0.802	0.073	9.1	0.026	3.24	0.879	0.088	10.0	0.023	2.61	0.840	0.064	7.61	0.010	1.42
	EF	0.772	0.054	7.0	0.0137	1.77	0.877	0.146	16.64	0.022	2.50	0.842	0.043	5.10	0.012	1.20
Mesial	CM	0.994	0.100	10.1	0.005	0.50	0.703	—	—	—	—	1.051	0.144	13.70	0.024	2.28
	CF	0.878	0.036	4.10	0.006	0.68	0.737	0.038	5.15	0.003	0.40	1.235	0.119	9.63	0.007	0.56
	EM	0.744	0.176	23.65	0.007	0.94	0.712	0.070	9.83	0.005	0.70	1.012	0.113	11.16	0.010	0.98
	EF	0.725	0.145	20.0	0.012	1.65	0.843	0.045	5.33	0.004	0.47	0.945	0.230	24.33	0.021	2.22
Bifurcation	CM	1.062	0.138	13.93	0.006	0.56	1.425	0.030	2.10	0.002	0.14	2.261	0.278	12.30	0.020	0.88
	CF	1.287	0.117	9.1	0.009	0.64	1.297	0.335	25.82	0.008	0.61	1.982	0.556	28.05	0.025	1.26
	EM	1.291	0.364	28.20	0.008	0.61	1.460	0.475	32.53	0.013	0.90	2.229	0.596	26.02	0.032	1.39
	EF	1.178	0.406	34.46	0.011	0.93	1.413	0.454	32.13	0.020	1.41	1.993	0.946	47.46	0.024	1.20

EM = Experimental male.
EF = Experimental female.
CM = Control male.
CF = Control female.

RL = Root length.
L = Length.
D = Depth.

TABLE III. SURFACE DISTRIBUTION OF CEMENTUM RESORPTION

SURFACE		LENGTH OF ROOT IN THIRD MOLARS (MM.)	AMOUNT OF RESORPTION: LENGTH (MM.)	AMOUNT OF RESORPTION: DEPTH (MM.)	PERCENTAGE RESORPTION: LENGTH	PERCENTAGE RESORPTION: DEPTH
Distal	C	2.654	0.273	0.086	10.28	3.24
	E	2.05	0.234	0.052	11.41	2.53
Mesial	C	2.801	0.212	0.020	7.56	0.71
	E	2.507	0.393	0.030	15.67	1.19
Bifurcation	C	4.634	0.803	0.037	17.32	0.79
	E	4.766	1.577	0.055	33.08	1.15

C = Control.
E = Experimental.

TABLE IV. SEX DISTRIBUTION OF DATA FROM TABLE III

SURFACE		ROOT LENGTH OF FIRST, SECOND, AND THIRD MOLARS (MM.)	AREA OF CEMENTUM RESORPTION		PERCENTAGE OF CEMENTUM RESORPTION	
			LENGTH (MM.)	DEPTH (MM.)	LENGTH	DEPTH
Distal	CM	2.706	0.298	0.068	11.01	2.51
	CF	2.625	0.259	0.115	9.86	4.38
	EM	2.521	0.225	0.059	8.92	2.34
	EF	2.491	0.243	0.048	9.75	1.92
Mesial	CM	2.748	0.244	0.029	8.87	1.05
	CF	2.833	0.193	0.015	6.81	0.52
	EM	2.468	0.359	0.022	14.54	0.89
	EF	2.513	0.420	0.037	16.71	1.47
Bifurcation	CM	4.798	0.456	0.028	9.50	0.58
	CF	4.566	1.008	0.042	22.07	0.91
	EM	4.970	1.435	0.053	28.87	1.06
	EF	4.574	1.806	0.055	39.48	1.20

CM = Control male.
EM = Experimental male.
CF = Control female.
EF = Experimental female.

TABLE V. TOOTH DISTRIBUTION OF CEMENTUM RESORPTION

TOOTH		ROOT LENGTH (DISTAL, MESIAL AND BIFURCATION) (MM.)	AREA OF CEMENTUM RESORPTION		PERCENTAGE OF CEMENTUM RESORPTION	
			LENGTH (MM.)	DEPTH (MM.)	LENGTH	DEPTH
Third molar	C	2.884	0.245	0.054	8.49	1.87
	E	2.764	0.546	0.039	19.75	1.41
Second molar	C	2.949	0.412	0.037	13.97	1.25
	E	3.095	0.641	0.043	20.71	1.38
First molar	C	4.256	0.631	0.052	14.82	1.22
	E	3.919	1.017	0.055	25.95	1.40

C = Control.
E = Experimental.

TABLE VI. SEX DISTRIBUTION OF DATA FROM TABLE V

TOOTH		ROOT LENGTH DISTAL, MESIAL AND BIFURCATION (MM.)	AREA OF CEMENTUM RESORPTION		PERCENTAGE OF CEMENTUM RESORPTION	
			LENGTH (MM.)	DEPTH (MM.)	LENGTH	DEPTH
Third molar	CM	2.832	0.292	0.022	10.31	0.77
	CF	2.916	0.217	0.073	7.44	2.50
	EM	2.837	0.613	0.041	21.60	1.44
	EF	2.675	0.605	0.0367	22.61	1.37
Second molar	CM	3.054	0.196	0.033	6.41	1.08
	CF	2.916	0.539	0.039	18.48	1.33
	EM	3.051	0.633	0.031	20.74	1.01
	EF	3.133	0.645	0.046	20.58	1.46
First molar	CM	4.316	0.510	0.068	11.81	1.57
	CF	4.192	0.704	0.042	16.79	1.0
	EM	4.142	0.773	0.052	18.66	1.25
	EF	3.780	1.219	0.057	32.24	1.50

CM = Control male.
CF = Control female.
EM = Experimental male.
EF = Experimental female.

TABLE VII. TYPE OF CEMENTUM RESORPTION AND REPAIR

TYPE OF RESORPTION	ANIMAL	TOOTH								
		THIRD MOLAR			SECOND MOLAR			FIRST MOLAR		
		DISTAL	MESIAL	BIFURCATION	DISTAL	MESIAL	BIFURCATION	DISTAL	MESIAL	BIFURCATION
Active repair	Control	18	3	3	41	x	4	20	7	13
	Experimental	53	13	18	63	9	52	34	18	73
Aplastic	Control	19	15	26	40	6	14	16	18	47
	Experimental	23	44	76	28	15	53	13	34	88
Active resorption	Control	20	3	5	15	2	8	9	2	23
	Experimental	x	10	8	7	4	17	2	3	19

TABLE VIII. SUMMARY OF TABLE VII

GROUP	TYPE OF CEMENTUM RESORPTION AND REPAIR						TOTAL NUMBER OF AREA STUDIED
	ACTIVE REPAIR		APLASTIC		ACTIVE RESORPTION		
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	
Control	109	27.45	201	20.62	87	21.91	397
Experimental	333	42.67	376	48.32	70	8.99	778

TABLE IX. STATISTICAL ANALYSIS OF TABLE I

	SURFACE					LEVEL OF CONFIDENCE
First molar	D	$= \frac{0.025}{0.0714} =$	0.35	Not significant	> 0.05
	M	$= \frac{0.145}{0.0714} =$	1.957	Significant	< 0.05
	B	$= \frac{0.266}{0.0761} =$	3.495	Significant	< 0.001
Second molar	D	$= \frac{0.1}{0.0748} =$	1.337	Not significant	> 0.05
	M	$= \frac{0.48}{0.0583} =$	8.233	Significant	< 0.001
	B	$= \frac{0.245}{0.0755} =$	3.245	Significant	< 0.001
Third molar	D	$= \frac{0.019}{0.0721} =$	0.263	Not significant	> 0.05
	M	$= \frac{0.3}{0.0735} =$	4.081	Significant	< 0.001
	B	$= \frac{0.311}{0.0755} =$	4.12	Significant	< 0.001

M = Mesial.
D = Distal.
B = Bifurcation.
> = Greater than.
< = Lesser than.

to surface and tooth involvement for both males and females are so inconsistent that they do not permit the drawing of any conclusions.

The different types of cementum resorption and repair and their location in both experimental and control groups are summed up in Tables VII and VIII. All three types (active repair, aplastic and active resorption) are seen in both groups. Active resorption seems to be greater (21.91 per cent against 8.99 per cent) in the control group, and the active repair type is more evident (42.67 per cent against 27.45 per cent) in the experimental group. There is very little difference in the occurrence of the aplastic type in both groups (50.62 per cent against 48.52 per cent).

DISCUSSION

The gross changes supported by microscopic changes in the soft tissues, observed in amount of experimental group, established the fact that a true vitamin A deficiency was present. Hyperplasia and hyperkeratosis of the epithelial layer of gingival tissue observed in vitamin A-deficient animals is in disagreement with the reports of Boyle and Bessey,[1] and Glickman and Stoller,[8] who found no such changes in vitamin A deficiency experiments, and is in agreement with the work of Mellanby[12] and King.[13]

Abnormal calcification, which is manifested by hematoxylin-staining globules in the periodontal membrane on the cementum side of the tooth and especially prominent near the cementoenamel junction, seems to be the same as was noticed by Schour and Van Dyke[9] in their hypophysectomized rats. On the basis of their suggestions, we can also explain this abnormal and pathological calcification of periodontal membrane fibers as a disturbance or enhancement of the normal phase in the calcification in cementum formation, caused by vitamin A directly or indirectly through changes in the metabolic or glandular function of the body.

The irregular narrowing of the periodontal space due to vitamin A deficiency in our animals is in agreement with the findings of Schour and associates.[10] Glickman and Stoller[8] have shown no changes in periodontal membrane, whereas Boyle and Bessey[1] have reported widening of periodontal membrane. The difference between these findings and those of Boyle and Bessey is most likely the result of the experimental approach. In their experiment, an acute vitamin A deficiency was produced in weanling rats and by restricting the vitamin A intake of mothers during pregnancy and lactation.

Since with loss of function there is narrowing of the periodontal membrane, this narrowing may also be attributed to loss of function of the molar teeth developed during the later period of vitamin A deficiency.

The changes in the alveolar bone observed in the experimental animals confirm the investigations of Boyle and Bessey[1] and Burn, Orten, and Smith.[11] This is in disagreement with the findings of Glickman and Stoller,[8] who reported no changes due to vitamin A deficiency. The increased osteoclastic

activity noticed in vitamin A-deficient animals in this study is contrary to the report of Mellanby[12] but agrees with King,[13] Sehour and associates,[10] and Wolbach and Bessey.[14]

Enhanced cementum resorption of statistical significance was observed in the vitamin A-deficient animals as compared to control animals and is in agreement with the work of Boyle and Bessey[1] and Burn, Orten, and Smith,[11] but is not supported by others.[2, 5, 6] It seems that the calcification of periodontal membrane fibers reported in this study may have been interpreted by these investigators as thickening of cementum. The ankylosis noticed in vitamin A-deficient animals may also be attributed to some disturbances in the metabolism and a pathologic calcification leading to an exaggerated reparative phenomenon.

Results of the findings in this study in relation to cementum resorption are clear enough to indicate that there was cementum resorption in both control animals and vitamin A-deficient animals and that the experimental animals showed an enhanced cementum resorption as compared to the controls.

These findings still strengthen our viewpoint that vitamin A deficiency increased osteoclastic and cementoclastic activity. Since in the rats there is a physiologic distal drift of the molar teeth, the finding that there is more cementum resorption on the distal surface than on the mesial surface is no surprise, but it is hard to explain why there is maximum resorption in the bifurcation. The reverse relation in the vitamin A-deficient animals, namely, that the mesial surface shows more cementum resorption than the distal surface, may be caused by some disturbances in the metabolic process and stress mechanism of the body and aggravated by local loss of function caused by a vitamin A deficiency.

The findings that the incidence of "active resorption type" is greater in the control animals and of the "active repair type" is greater in vitamin A-deficient animals are misguiding and likely to be misinterpreted. These findings represent only the incidence in the number of areas counted and do not show the amount of cementum resorption in quantitative terms. The higher incidence of the presence of "active repair type," as has already been stated, may be an exaggerated reparative phenomenon caused by metabolic disturbances of the body due to vitamin A deficiency.

CONCLUSIONS

1. Periodontal structures of rat molars show hyperkeratosis and hyperplasia of the gingival tissue, atrophy of the alveolar bone, calcification and irregular narrowing of the periodontal membrane, excessive cementum resorption, and ankylosis of teeth due to vitamin A deficiency.

2. There is more cementum resorption in the group of rats on the vitamin A-deficient diet than in the control group.

3. The difference in the amount of cementum resorption in the two groups is of statistical significance (0.05 level of confidence) on both the mesial and

the bifurcation surfaces, while the cementum resorption on the distal surface is not significantly different between the two groups.

4. There is maximum cementum resorption in the bifurcation area in both vitamin A-deficient and control animals.

5. In the vitamin A-deficient group the distal surface has the least amount of cementum resorption, while in the control group the mesial surface has the least amount of resorption.

6. The first molar shows maximum cementum resorption, and the third molar shows the least. This holds true for both vitamin A-deficient and control groups.

7. Sex seems to play no part in cementum resorption.

The author offers his deep and sincere appreciation to Dr. Helmet A. Zander for his guidance and help in carrying out this work. Thanks are also due to Miss Francis McCandless and Mrs. Ivanow for their technical help.

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ARMED FORCES AND PUBLIC HEALTH SERVICE

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TRENDS IN MAXILLOFACIAL SURGERY IN ACUTE TRAUMA

*Charles C. Alling, Lieutenant Colonel, DC, USA**

THE concept that continuous and continuing education is necessary for the professional man and the attitude of trust and respect that communities in the United States give to the dental profession make necessary a periodic review of the role that dentistry is playing in the treatment of maxillofacial injuries caused by acute trauma. In the spirit of periodic review, I will emphasize the various aspects of the early phases and note the trends in the intermediate and late phases of treatment of oral and facial injuries.

Battlefield injuries and civilian accidents involving high-speed land and air transportation have contributed to increasing complex trauma patterns during the past four decades. The principles of treatment of maxillofacial soft and osseous tissue injuries, however, and the rules for evacuation of patients have not been changed but rather have been reinforced by these complicated traumatic injuries. For example, more than two millenniums ago Hippocrates stated that the principles of treating fractures were, in essence, reduction and alignment of the fractured parts and maintenance of these bony segments in apposition until healing had occurred. These principles are as fundamental today as they were in Hippocrates' time. Likewise, the classical lines of fractures of the mandibular and middle thirds of the face, as described by Le Fort[2] (Fig. 1), are still fundamental in diagnostic evaluation and treatment planning. Of course, the increased severity seen today, as a result of the use of destructive weapons and fast transportation, often causes fractures along any combination of several of the fracture lines of the mandibular and middle thirds of the face. Fortunately, advances in surgical technique, therapeutics, and anesthesia have given us effective methods of managing injuries to the oral cavity and contiguous areas (Fig. 2). These advances in the disciplines of oral surgery in the United States have been

From lectures to the 1958-1959 Graduate and Postgraduate Courses in Oral Surgery, Letterman Army Hospital.

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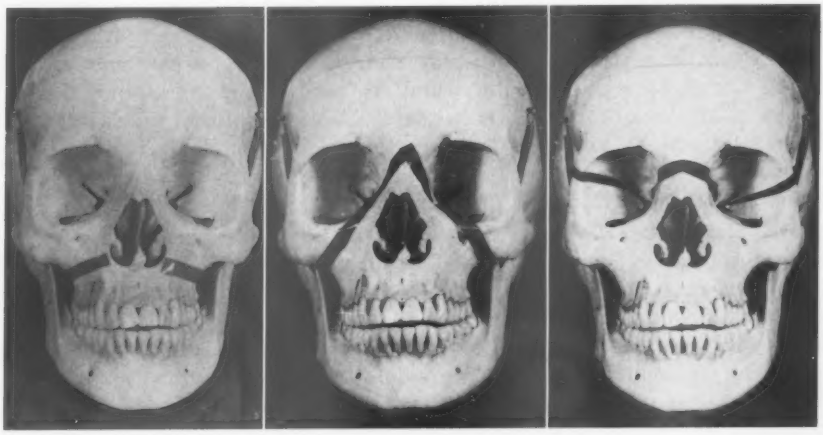
brought about by the unselfish dedication of men with ability, vision, and leadership who, in the early and middle nineteenth century, established oral surgery as a specialty and who, in the first half of the twentieth century, have administered residency training programs in the leading civilian and military hospitals, created the flourishing American Society of Oral Surgeons, developed the respected American Board of Oral Surgery, and supported oral surgery literature in textbooks and journals.[3-8] A vast number of civilian and military patients have benefited from these evolutionary developments of oral surgery, including the advances made in the treatment of maxillofacial injuries following acute trauma.

EARLY PHASES

As a very general rule, maxillofacial injuries are not acute surgical emergencies except as they influence asphyxia and hemorrhage. Prompt and effective attention must be directed to the correction of these latter conditions.



A. *B.* *C.*

Fig. 1.—*A*, Le Fort fracture I, a bilateral transverse line of fracture of the maxillae. *B*, Le Fort fracture II, a pyramidal line of fracturing of the maxillofacial bones. *C*, Le Fort fracture III, a fracture separation of the cranial and facial bones. *(U.S. Army photographs.)*

Experiences and writings emerging from the two world wars and the Korean conflict emphasize the basic necessity of guarding against respiratory obstructions.[9-12] Occlusion of the airway may be induced by blood clots in the pharyngeal regions or by foreign bodies, such as avulsed teeth, torn bits of soft tissue, bone fragments, dental prostheses, and extraneous matter that may have been blasted or forced into the oral or nasal cavities. Blockage of the pharyngeal air space may be caused by the tongue falling back in response to fractures of the anterior mandible or lacerations at the base of the tongue which prevent control of the protruding action of the genioglossus muscle.[13] If respiratory obstruction is obvious or impending, the tongue

should be grasped and pulled forward and the pharynx cleared of foreign bodies with the fingers, pick-up instruments, and suction. Future respiratory

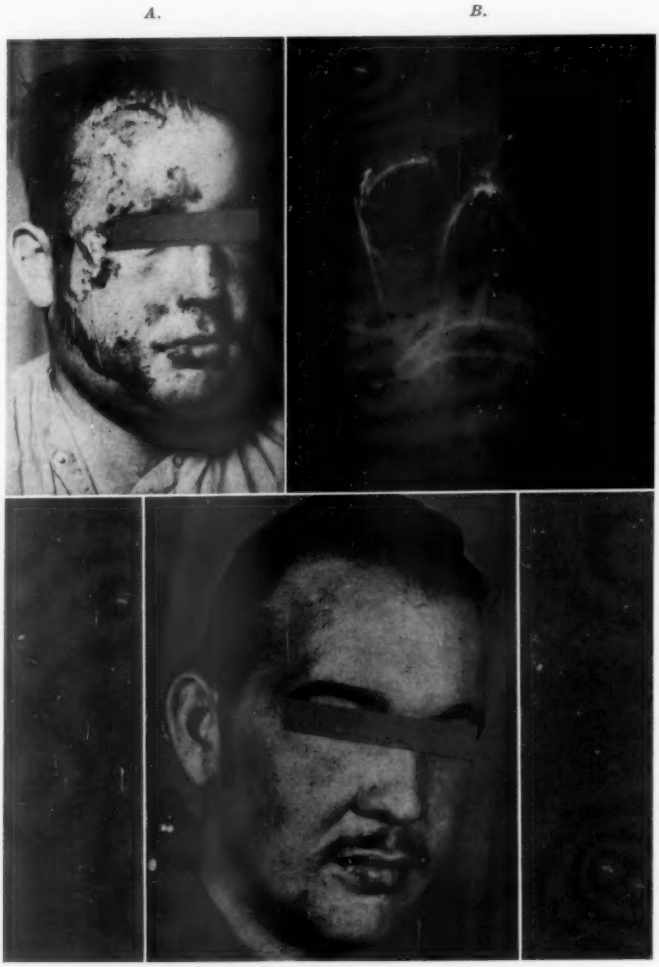


Fig. 2.—*A*, Photograph of patient who was involved in an airplane accident and incurred a bilateral transverse fracture of the maxillae and a pyramidal fracture of the facial bones, that is, Le Fort fractures I and II. The mandible was not injured.

B, Treatment included bilateral internal craniofacial suspension from the zygomatic processes of the frontal bone to a mandibular labial arch bar and bilateral open reduction of the malar-maxillary suture lines via infraorbital incisions.

C, Eight months following surgical correction.

(U.S. Army photographs.)

obstructions may be prevented by the use of a properly placed oral or nasal airway; by placing the patient in a prone or side position with his face pointing downward or to the side so that gravity will prevent mucus, blood, and

foreign objects from pooling in the pharynx; and by the use of various devices, such as safety pins, towel clips, and ligatures, which, in turn, may be fastened to the patient's clothing or held by an attendant.

The necessity for tracheostomy must be weighed in practically every patient with a maxillofacial injury. It is of interest to recall the observations by Chipps and colleagues[10] concerning the liberal use of tracheostomies in 1,000 osseous maxillofacial injuries treated during the Korean conflict; there were no deaths due to asphyxiation even though there was frequent use of air evacuation, often in helicopters with no one attending the patients. This serves to emphasize the contention that tracheostomy should rarely be an emergency procedure but that it usually should be a prophylactic, preventive measure. An airway directly from the trachea may be provided on an emergency basis by a fairly formal surgical procedure consisting of a midline dissection by layers and a longitudinal incision through the second and third tracheal rings, a horizontal incision through the cricothyroid membrane, or the insertion of one to several 13 gauge needles in the upper tracheal apparatus.[14-16] Shelden and his colleagues[17] made a signal contribution by devising an instrument for performing a tracheostomy in a few simple movements (Fig. 3).

Hemorrhage usually is not a pressing danger in maxillofacial injuries except as it affects the airway. Pressure dressings, closure of lacerations, and immobilization of facial-bone fractures will correct most hemorrhage problems in the oral and facial areas. Hemorrhage of the internal maxillary artery may be quite profuse and, because of its position in the infratemporal fossa, inaccessible to corrective procedures. Ligation of the external carotid artery may become necessary and should be performed in lieu of a blind and futile search for the internal maxillary artery. The same approach could apply to hemorrhage in the distribution of the lingual artery. Ligation of the lingual artery at Lesser's hypoglossal triangle is said to give positive control of more peripheral vascular lacerations,[18] but a cut-down procedure to the external carotid artery will give the operator control in a lingual vascular emergency by a less complicated operation (Fig. 4).

Burns to the face, oral, pharyngeal, and nasal spaces are of immediate concern in that they may affect respiration by causing an edema that will rapidly occlude the airway. This emergency should be met with a tracheostomy. The care advocated for burns of the facial tissue during the first weeks following injury includes exposure to air with removal of excreted fluids by means of the gentlest possible sterile sponging and suction.[19]

Immediately after the airway and hemorrhage problems have been assessed and controlled, a general physical examination by the best-qualified person available should be performed with emphasis on the neurologic, abdominal, and ophthalmologic aspects. Following or during this examination, a complete investigation of the facial-bone fractures may be performed.

Most of the lines of fractures of the facial bones can be plotted by inspection and palpation. The dental arches, occlusal relations, movements of the mandible, and intraoral and extraoral contusions and lacerations will indicate the fractures of the mandible. A cellulitis about the mandible may

limit the usefulness of extraoral palpation, but usually the entire body of the mandible and the anterior border of the ascending ramus may be palpated intraorally. Suspected fractures of the condyle or subcondylar necks of the

Fig. 3.

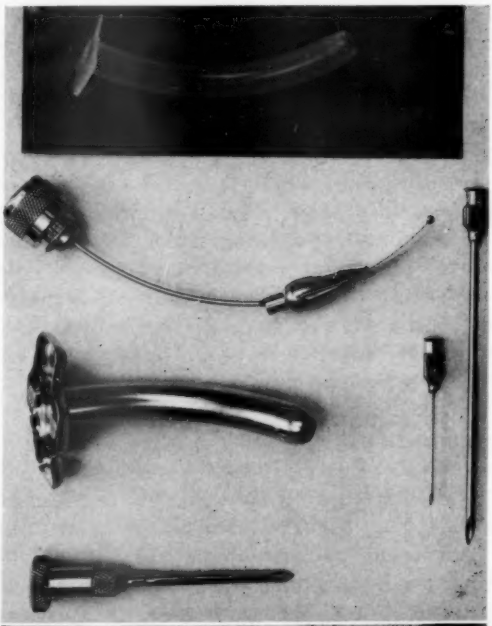


Fig. 4.

Fig. 3.—*Left:* The component parts of a Shelden type of tracheosteotome. *Right:* A 13 gauge injection needle with a 21 gauge injection needle beside it for comparison.

Fig. 4.—A cut-down procedure to the external carotid artery was performed through this incisional line to control a hemorrhage of the internal maxillary artery.

(U.S. Army photographs.)

mandible may be investigated by palpation at the lateral aspects of the condylar heads; suspected fractures at the posterior aspects may be investigated by palpation in the anterior portion of the external auditory meatus. Also, a light percussion on the symphysis of an otherwise intact mandible will elicit pain in the area of injury to the heads or necks of the mandibular condyles.

Examination of the middle third of the face should begin with inspection and bimanual palpation of the zygomatic arches, the orbital rims, and the nasal bones to establish the presence or absence of fractures of the zygomatic arch, the malar bone, and the nasal bone. Then, proceeding to the oral cavity, observation of the dental occlusal relations, inspection of the dental arches, and the finding of intraoral contusions and lacerations contribute to a determination of the extent of injury. Further information may be gained from the intraoral examination by palpating along the buttresses of the malar bones and around the bodies, tuberosities, and alveolar processes of the maxillae. If these procedures have established that bony injuries involve the maxillae, one may then grasp the maxillae intraorally and exert gentle movements; observation and palpation with the other hand over the nose, the orbital rims, and the zygomatic arches will disclose the extent and lines of fracture.

Various roentgenographic examinations are considered to substantiate the clinical impressions, to ascertain extensions of the lines of fracture in the bony wall of the infratemporal space and on to the cranial bones, and to delineate occult fractures. For the mandible, we have the following views: (1) projections of the temporomandibular articulation, (2) ramus of the mandible, (3) body of the mandible, (4) posteroanterior mandible, and (5) a rotated posteroanterior mandible projection for the symphysis area. Injuries to the maxillae, malar bones, nasal bones, and zygomatic arches are demonstrated on the following projections: (1) lateral skull exposed for the facial bones, (2) posteroanterior skull, (3) basilar skull, and (4) paranasal sinus views. Stereoscopic pictures are often useful for the latter four projections. In many of the preceding, we may desire an anteroposterior projection or have to accept this projection in the event a bedside examination with portable roentgenographic equipment is necessary due to the patient's being in orthopedic or some other type of traction. It may be advisable to seek consultation with the roentgenologist when ordering the projections, as he can alter alignments to emphasize given portions of the craniofacial bones and utilize different nonstandard positions to demonstrate various fractures. The preceding roentgenographic examinations can be made with a dental roentgenographic unit, which is a convenience for the ambulatory patient and may be an important Civil Defense consideration in planning for contributions of the dental office in the management of mass casualties in a disaster situation.[20] In addition to the extraoral surveys, the standard periapical and occlusal roentgenograms that demonstrate details of the alveolar processes and dentition are of inestimable value in determining the fate of a tooth in or near a line of fracture.

It is desirable to institute definitive therapy as soon as possible after the injury, but not before the patient's general condition warrants. A delay in treatment of patients who have maxillofacial injuries with associated central nervous system injuries is indicated until a neurosurgical consultant has given his clearance. During World War II it was discovered that if a patient is not in a state of shock, cerebrospinal rhinorrhea is not a contraindication to facial-bone surgery.[21] Spinal rhinorrhea usually will cease in a matter of hours following gentle but anatomic reduction and immobilization of fractured facial bones against the cranial components when the operation has had a neurosurgical clearance.

The dental occlusal relations and the application of fracture appliances to the dental arches are the key to accurate reduction of the great majority of maxillofacial osseous injuries. It is often necessary to make impressions of the dentition for the study of interdental relationships and/or the construction of indicated applicances. Entrance to the oral cavity for taking the required impressions often is easier prior to the closure of the soft-tissue injuries, and an intraoral fracture appliance can be placed most conveniently and without damaging newly closed lacerations prior to the primary repair of the soft-tissue injuries. For this reason, support is given to Irby's[22] advocacy of delaying the soft-tissue repair for as much as forty-eight hours in a certain few cases if necessary for placing complex intraoral fracture appliances. It may be expedient to carry out an open reduction of a facial-bone fracture with direct transosseous wiring through the soft-tissue laceration; this procedure gives very satisfactory results, particularly when intermaxillary fixation is used concurrently.

Débridement of the facial tissues should be markedly limited, as compared to other areas of the body, and should consist of copious irrigations with normal saline by gentle sponging of the injured tissues; all tags of attached soft and bony tissue following this wet débridement are retained (Fig. 5). In the closing of facial soft-tissue lacerations the usual general surgical principles of asepsis, control of hemorrhage, and closure by layers prevail. Sometimes it is suggested that oral mucosal lacerations should not be closed because of the possibility that mucous retention cysts may be created. This remote possibility is far outweighed by the probability that contamination will enter the laceration from the flora of the oral cavity if the laceration is allowed to persist with closure of only the external subcutaneous tissue and cutaneous surface. Furthermore, inaccurate and inadequate control of intraoral lacerations will result in disfiguring external facial scar contractures and intraoral cicatricial deformities that will preclude normal masticatory movements or the wearing of a dental prosthetic appliance.

The parotid duct, crossing lateral to the masseter muscle and parallel and 1 to 2 cm. below the zygomatic arch, requires special care during the closure of facial lacerations. Failure to reapproximate the duct may lead to a troublesome fistula (Fig. 6). This complication is readily avoided at the

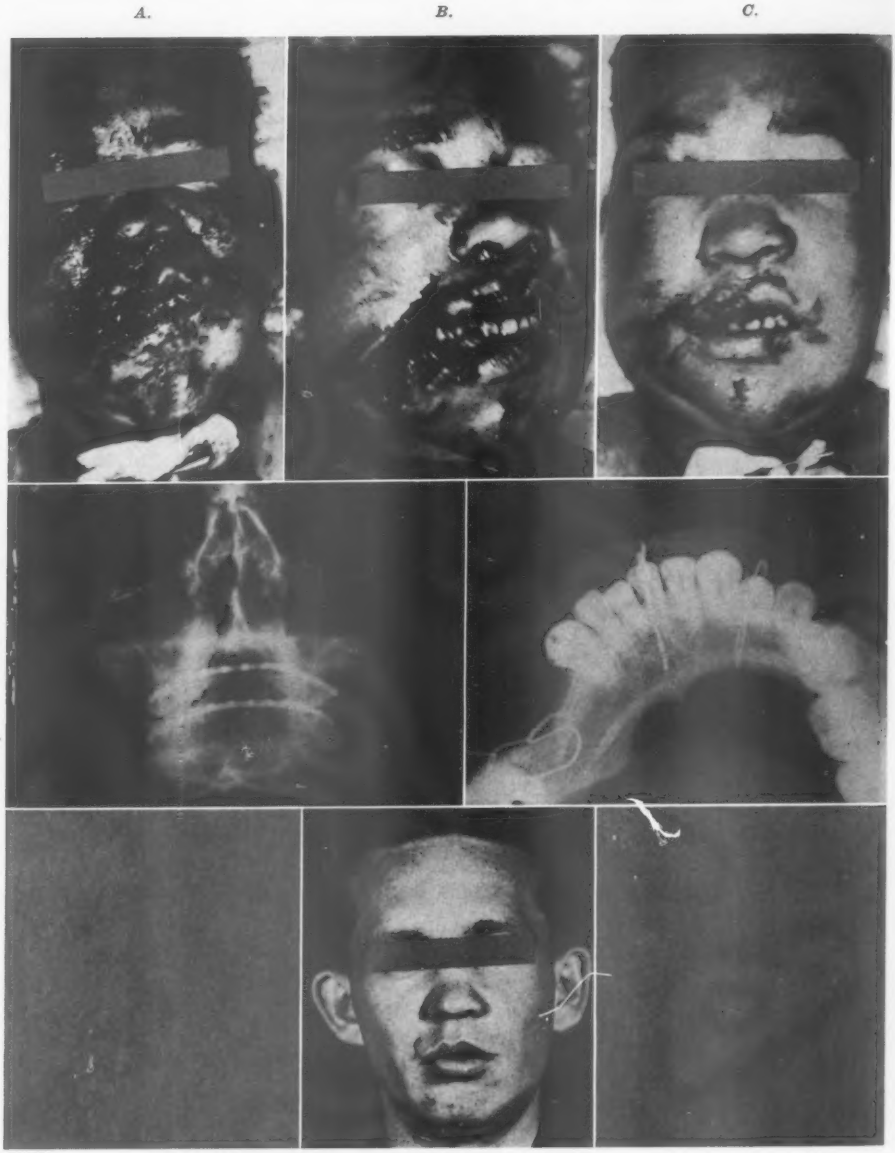


Fig. 5.—*A*, Facial appearance forty-five minutes following an automobile accident. (Note that a tracheostomy has been performed.) Patient has incurred a pyramidal fracture on the left and a crush fracture of the right middle third of his face. There has been an avulsion of 2 cm. of the body of the right mandible. There are a profound concussion, cerebrospinal rhinorrhea, a cervical vertebral fracture, and multiple fractures of his legs.

B, Facial appearance following wet débridement.

C, Facial appearance following closure of the soft tissues.

D, Five days following admission, open reduction, internal craniofacial suspension from the orbital rims, and intrasinal elevation of the walls of the right maxilla were performed. The cerebrospinal rhinorrhea ceased a few hours following the operation.

E, Due to the patient's precarious condition, bone-graft correction of the mandibular defect was not performed, and a right unilateral shortening of the body of the mandible was accepted. Since the resultant occlusal relations were functional, the mandible was recontoured by onlay bone grafts from the iliac crest rather than by lengthening the body of the mandible. This operation was performed six months following the original injury.

F, Facial appearance twelve months following original injury.

(U.S. Army photographs.)

time the laceration of the adjacent tissues is repaired. For example, an inlying plastic catheter introduced from the oral cavity opening of the duct, spanning the laceration, and entering the proximal portion of the duct will allow satisfactory repair of the duct, particularly if 000000 silk sutures are placed by means of an atraumatic ophthalmology needle to help approximate the lacerated ends of the duct. Another method of repairing the duct consists of placing a monofilament nylon suture through the soft tissues anterior to the laceration, entering the distal lumen of the duct, spanning the laceration, entering the proximal lumen of the duct, and then passing the suture through the duct wall and up to the cutaneous surface posterior to the laceration; the duct can be threaded together on this central suture and immobilized by routine closure of the surrounding soft tissues and by tying the ends of the central suture on the face.

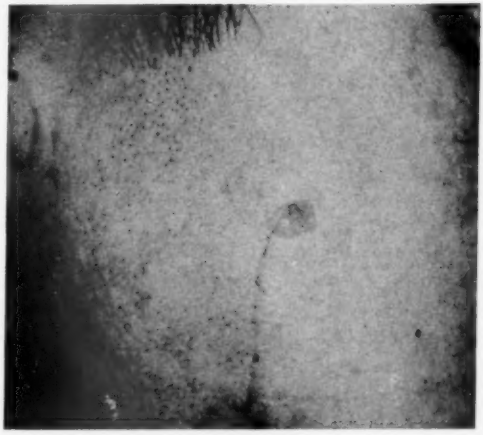


Fig. 6.—Repair of a facial laceration without repair of the parotid duct resulted in this parotid-cutaneous fistula. *(U.S. Army photograph.)*

Most soft-tissue injuries of the face are contaminated by the wounding object or by the flora of the oral cavity. Since most injuries of the facial bones are compound fractures into the oral cavity, the correct systemic and oral topical antibiotics[23] and antitetanic drugs should be given in adequate doses to prevent infections. If there is a cerebrospinal rhinorrhea, sulfonamides and/or chloramphenicol should be used for prophylaxis against infection. There is a place for the use of hyaluronidase to decrease the edema accompanying the reaction to the injuring agent.[24] Enzymatic débridement, a product of research development, is undergoing clinical application that may have increasing usage in the future.[25] There also may be indications for the use of antihistaminic drugs to forestall allergic reactions to other drugs or agents being used,[26] as well as for their antiemetic action.[27] The operating team should be prepared to administer blood replacements or plasma-volume

expanders, since injuries and operations to the facial area are somewhat shocking in character from both the neurogenic and the hematogenic standpoints.

Following adequate premedication with barbiturates, morphine or meperidine, and atropine or scopolamine, many of the less severe maxillofacial injuries may be managed under local anesthesia by skillful regional block of the involved nervous network. In the very extensive injuries, however, the procedure is easier for both the surgeon and the patient if general anesthesia is used. In this instance, it is advisable to guarantee the patency of the airway by introduction of an intratracheal tube.

INTERMEDIATE PHASES

It is convenient and logical to divide treatment of maxillofacial osseous injuries between fractures of the mandibular and middle thirds of the face. This is logical because the intact or reconstructed mandible usually provides the key to accurate repositioning of fractures of the middle third of the face by correctly occluding the dentition or reconstructing the oral cavity as a part of the treatment.

The various methods of effecting a closed reduction and immobilization of mandibular fractures are usually dependent upon correct alignment of the dentition in the occlusion that existed prior to injury, thereby effecting an anatomic realignment of the fractured segments. Most maxillofacial injuries that consist primarily or solely of a fractured mandible can be managed by closed reduction. One group of closed-reduction methods of treatment depends upon splints or bars that bridge the fracture site and hold the involved fragments in position until repair ensues. Examples are the full cast-metal splints that cover the coronal portions of the teeth, sectional splints that rely on undercuts in the dental arches for stability, lingual or labial splints that are wired to the dentition, manufactured labial arch bars, bars formed by wiring techniques using stainless steel wire, denture or denturelike splints for circumferential wiring in the edentulous patient, and various external pin fixation devices (Fig. 7). Another group of closed-reduction methods is dependent upon appliances equipped with lugs for intermaxillary elastic traction or wire fixation. Examples are the single- and multiple-loop wiring techniques, manufactured labial arch bars, and plastic or metal splints cast for the individual case (Fig. 7).[28-30] Of course, combinations of the various methods are used as indicated by the requirements of each case.

If the fractured parts of the mandible are so severely displaced by trauma or muscle pull that intraoral appliances alone would not effect reduction and immobilization, if there is an interpositioning of soft tissue at the fracture site, or if the bone is comminuted, then an open reduction with direct vision of the fracture site offers a result which is superior to that obtainable with intraoral appliance only. The principal exceptions to these indications for open reduction of mandibular fractures are cases in which there is a loss of substance of the mandible and the area must undergo preparation for a

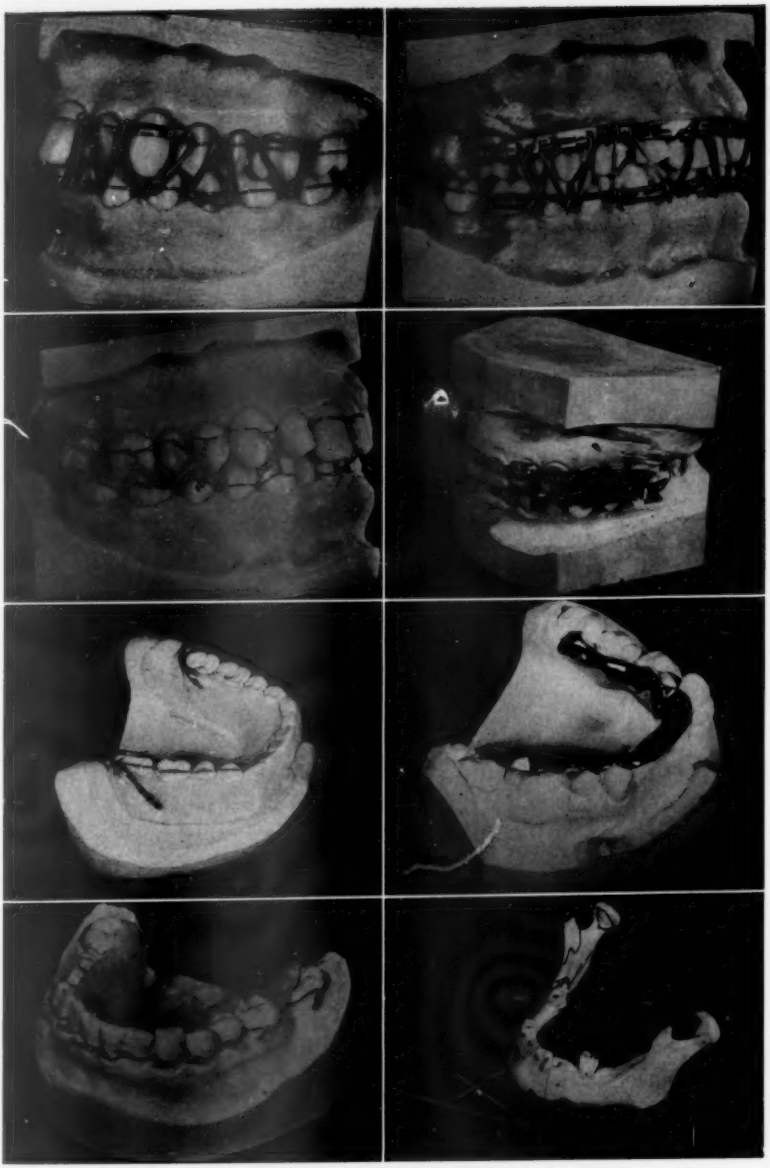


Fig. 7.—Methods and appliances for closed reduction of mandibular fractures.

A, Stout's continuous loop wiring.

B, Labial arch bar on the maxillary dental arch and Risdon arch on the mandibular.

C, Intermaxillary wire ligation.

D, Cast-cobalt-chromium arch bars.

E, Sectional plastic splint.

F, Lingual cast-gold splint.

G, Lingual plastic splint; note the occlusal support for stabilization on both the metallic and plastic lingual splints.

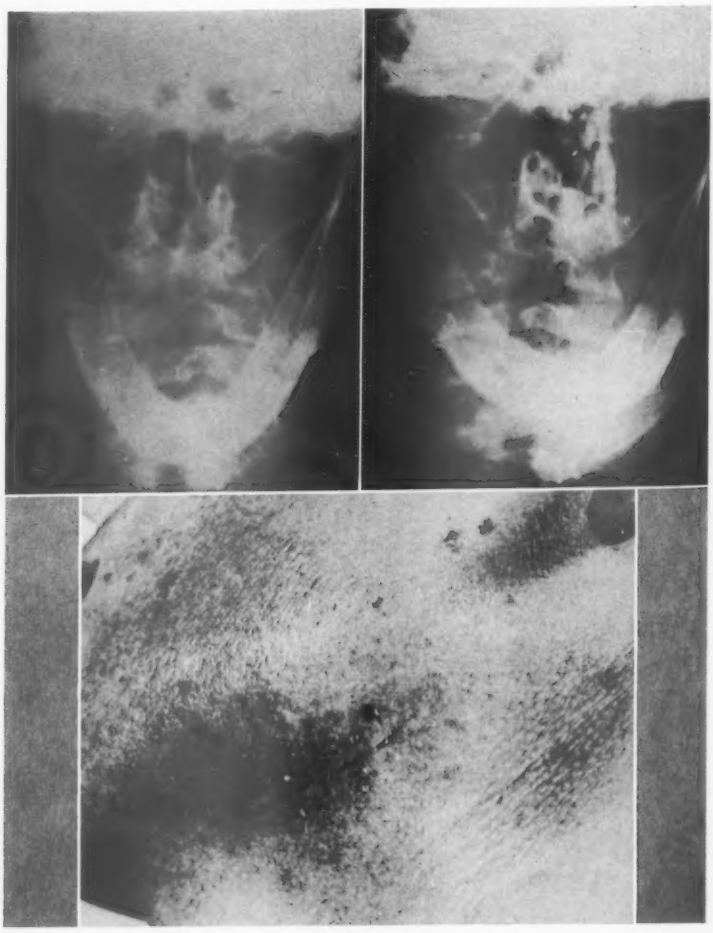
H, Roger-Anderson external skeletal fixation.

(Many of these appliances are from demonstration models prepared by Captain Charles Beard, DC, formerly of William Beaumont Army Hospital.)

(U.S. Army photographs.)

bone graft replacement, fractures of the coronoid processes which usually may be permitted to go unreduced, and fractures of the necks of the condyles that are *less severe* than bilateral fracture dislocations. When an open reduc-

A.



B.

Fig. 8.—*A*, Fractures of the left angle and right body of the mandible were treated by an extraoral open reduction on the left and intraoral open reduction on the right with direct transosseous wiring.

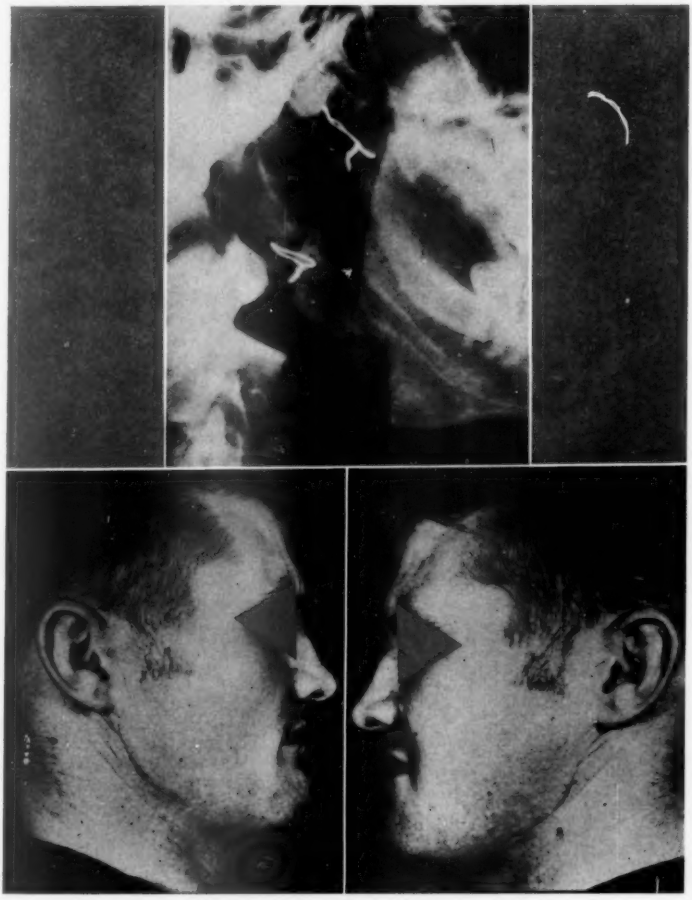
B, Skin incision in the shadow of the mandible ten days following open reduction with transosseous wiring.

(U.S. Army photographs.)

tion is indicated for any site on a fractured mandible, however, then the technique will involve the use of either direct transosseous wiring, small orthopedic bone plates, plates fabricated for the case at hand, or intramedullary

pin fixation. All these methods of open reduction should be combined with a closed-reduction appliance for optimum results (Figs. 8 and 9). The dominant method for open reduction is the judicious placement of transosseous stainless steel wiring.[31-34]

A.



B.

Fig. 9.—*A*, Bilateral fracture of the subcondylar necks of the mandible reduced by direct transosseous wiring and immobilized by intermaxillary fixation.
B, Skin incisions at the angles of the mandible eight days after surgery.
(U.S. Army photographs.)

For support of fractures of the middle third of the face that involve the masticatory apparatus, external craniofacial appliances have been used extensively and successfully. These appliances consist of three components: (1) the anchoring portion, which is either a leather or plaster headcap, a frame

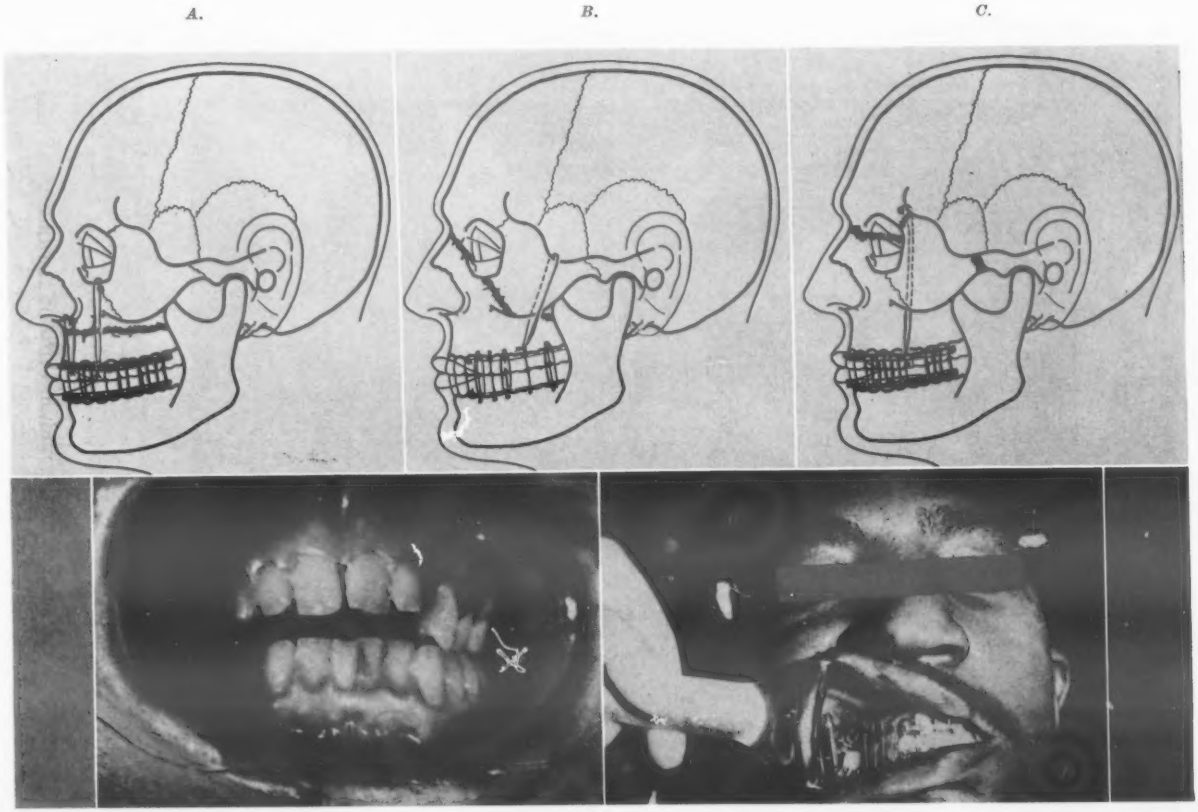


Fig. 10.—*(For legend, see opposite page.)*

inserted into the outer cranial bony plate, or a neck and body cast or frame; (2) the connecting portion, which either pierces the cheeks to enter the oral cavity or inserts through the oral orifice; and (3) the oral portion, which is fastened to the maxillary and/or the mandibular dentition by any of the methods described above under closed-reduction techniques.[35-38] Some of these external craniofacial fracture appliances offer sound methods for immobilizing facial-bone fractures, particularly when combined with support to the patient's shoulders in a Forrester frame or a full-head cast which prevents impaction of the lines of fracture of the delicate facial bones that could produce a superior displacement of the maxillae. The exact positioning of the maxillae in all these methods is obtained by moving them into normal occlusion with mandibular teeth.

The principles of internal wiring fixation for facial-bone fractures as described by Adams[39] have been of invaluable aid in producing exceptionally successful results. This technique, as well as modifications of it, consists of placing bilateral drill holes in the zygomatic processes of the frontal bone, in the infraorbital rims, or in the anterior rim of the bony nares or nasal spine, and then passing wires downward through the facial tissues and attaching them to dental arch appliances; this permits a suspension of the fractured facial bones against superiorly located intact bones.[34, 40, 41] If the anterior roots of the zygomatic arches are not injured, then circumferential wires may be passed with the ends emerging in the oral cavity and providing the necessary points of suspension.[42] One has to guard against superior overclosure into the lines of fracture when internal craniofacial suspension is used. As with external suspension, the exact positioning of the maxillae is obtained by moving them into a position of normal occlusion with the mandibular dentition (Fig. 10).

Several recent papers have summarized the various approaches to elevation of depressed fractures of the malar bone.[43-46] If there is minimum comminution of the fracture lines, and if there are no associated fractures of the maxilla, then one of the many variations of approaches and types of instruments devised for elevation of the malar bone by pressure on its infratemporal surface may be selected. The approaches are via either an intraoral incision, a buccal cutaneous puncture or incision, or a temporal hairline incision.[47-53] When an elevating manipulation will not suffice to correct a

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Fig. 10.—*A*, Transverse fracture of the maxillae immobilized by support from the infraorbital and infranasal rims and positioned by the mandibular dental occlusal relations.

B, Pyramidal fracture of the maxillofacial bones immobilized by circumferential wires around the anterior portion of the zygomatic arches and positioned by the mandibular dental occlusal relations.

C, Craniofacial dysjunction reduced by support from the zygomatic processes of the frontal bone and positioned by the mandibular dental occlusal relations.

D, Left: The patient incurred transverse fractures of the maxillae and a pyramidal line of fracture of the middle third of the face; the mandible is intact. *Right:* Treatment included craniofacial internal suspension from the frontal bone and positioning according to the mandibular occlusal relations. The two wires that protrude from the lateral aspects of the eyebrows are looped around the suspending wires and will assist in the removal of the latter.

(U.S. Army photographs.)

depressed malar fragment, then open reduction with direct transosseous wiring via eyebrow or infraorbital incisions offers positive control of the fragments without violating the maxillary antrum with its delicate lining membrane.[34] For severely comminuted fractures of the malar bone, intrasinal

Fig. 11.—*A*, Depressed fracture of right zygoma.
B, Open reduction and transosseous wire fixation on the infraorbital bony margin.
C, Postoperative roentgenogram demonstrates an anatomic alignment.
D, Facial appearance two weeks following surgery.
(U.S. Army photographs.)

elevation and molding of the fragments through a canine fossa approach followed by support of the bone fragments with an air-filled sinal balloon or a fluid-filled hemostatic bag catheter gives highly successful results (Fig. 11).[54-56]

Fractures of the zygomatic arch may be corrected by molding the arch into its desired curve with instruments introduced from the oral cavity, the temporal hairline, or directly over the arch. The belly of the temporalis muscle will hold the arch in its corrected contour, and the temporalis fascia will tend to prevent the arch from being displaced inferiorly. Following correction of fractures of the zygomatic arch and/or malar fractures, intraoral immobilization is indicated for two to four weeks to reduce the possibility of secondary displacement by muscle pull.

Nutrition is a most important factor in the general care of the patient with fractures of the maxillofacial complex of bones, particularly during the intermediate and final phases of treatment. It is rarely necessary to extract a tooth to maintain space for the adequate intake of nourishment when the mandible is immobilized against the maxillae, since there is enough space between the teeth and around the distal ends of the dental arches to permit the ingestion of liquid diets.[57] If possible, a dietitian should be consulted, since considerable ingenuity is required to keep the necessary high-calorie, high-vitamin, high-protein liquid diet varied and attractive for the patient. The use of a mechanical food liquidizer simplifies this aspect of the management of fractures. Chipps,[10] treating war injuries, and Henny,[58] concerned with civilian injuries, have noted the efficacy of stomach-tube feedings.

FINAL PHASES

The last phases of treatment may be as simple as releasing the intermaxillary traction, placing the patient on successively more firm diets, and obtaining occlusal equilibration and prosthodontic appliances, or this last phase may involve bone- and skin-grafting procedures and extend over a period of years. Prior to the rebuilding of the bony features, it is usually necessary to await completion of the skin-grafting replacement of defective areas of soft tissues. Bone grafts to restore bone continuity and function have been used through the ages, and iliac autoplastic grafts are currently in favor.[59] To restore bone contours and prominences, both bone and cartilaginous grafts have been advocated. There have been significant offerings of the use of artificial materials in this field; Shevick[60] reported using polyethylene subperiosteal implants to restore the chin contours, and Gerry and Giotta[61] presented a method of using tantalum plates.

Intraoral reconstruction of the dental arches by various prosthodontic appliances must be closely integrated with the plastic and reconstructive procedures that are being performed. It is of interest to note the progress of subperiosteal mandibular implant dentures in the practice of prosthodontics[62, 63] and Thoma's[41] report on the use of a subperiosteal mandibular implant over a bone graft in a case of mandibular reconstruction.

DISCUSSION

The general care of patients with fractures of the facial bones ordinarily should consist of the therapy considered desirable for any other traumatic case. First-aid methods include control of hemorrhage, establishment and maintenance of an airway, and prevention and treatment of shock. If it is not possible to effect immediate reduction of fractures of the facial bones, then support by head bandages will make the patient more comfortable, partially immobilize the fractures, and control any tendency to hemorrhage.

Open reduction and internal wire fixation provide a means of accurate, complete restoration of anatomic relation and immobilization of fractures of facial bones. The advantage of open reduction is that it eliminates the need for cumbersome external appliances and complicated intraoral splints, and open reduction of facial bones may be carried out through cutaneous incisions in inconspicuous locations. The mandible is essential as a guide for repositioning in cases of fractures of the middle third of the face, and if the mandible is fractured its reconstruction should precede reduction and correction of fractures of the middle third of the face.

Teamwork and cooperation are the essence of successful treatment of complex maxillofacial injuries.[1, 57] Because of the many combinations of primary injuries and subsequent complications, and because in different locales there will be a wide variance in interests and training of the representatives of the various specialties of the medical and dental professions, an attempt at precise definitions of responsibilities of the team members is tantamount to an invitation to failure in treatment management. Suffice it to say that ethical specialists of both medicine and dentistry, men of maturity who have the proper background of training and experience, are needed if the ultimate in results in the care of patients is to be achieved. For example, in an atmosphere of mutual respect and confidence, completed cases often will show contributions of talent from the realm of oral surgery, with assistance and advice from the specialties of prosthodontics and periodontics. In addition, active cooperation and consultations are sought and received from specialists in the fields of neurosurgery, plastic surgery, orthopedic surgery, otorhinolaryngology, ophthalmology, radiology, dietetics, psychology, and sociology.

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NEW DIRECTOR AT ARMED FORCES INSTITUTE OF PATHOLOGY

Colonel Frank M. Townsend, USAF, MC, has been appointed Director of the Armed Forces Institute of Pathology, succeeding Captain William M. Silliphant, MC, USN. Colonel Townsend is the first Air Force officer to assume the directorship of the Institute.

COLONEL FRANK M. TOWNSEND.

The Armed Forces Institute of Pathology is the central laboratory of pathology for the Department of Defense. In addition to serving the Armed Forces, the Institute meets the needs of the Public Health Service, the Atomic Energy Commission, the Veterans Administration, other Federal agencies, and civilian pathologists through its consultative service.

Colonel Townsend, the senior pathologist of the Air Force, also serves as the consultant in pathology to the Surgeon General, Department of the Air Force. The new Director is a pioneer in the field of aviation pathology.

EDITORIAL

FIRST CONFERENCE OF THE INTERNATIONAL ACADEMY OF ORAL PATHOLOGY

THE first conference of the International Academy of Oral Pathology, held at the New York Academy of Medicine on Sept. 15, 1959, gave clear evidence of the value and desirability of such an effort.

Forty-one oral pathologists, representing ten countries, met in an informal conference to discuss and exchange views on common problems. From these deliberations, it became evident that there is great need for new definitions and a broader approach to the understanding of many oral diseases.

In the discussions on "Conditions Which Predispose the Oral Mucosa to Cancer," it was suggested that the influence of infection, trauma, and nutrition can be more clearly defined on the basis of data which must be laboriously collected from the world's scientific literature, particularly publications of recent years. That there is a need for this is self-evident, and the Academy will no doubt make this one of its major efforts.

Similarly, it was the opinion of the conference members, after assessing the relationship between odontogenesis and neoplasia, that a better correlation of existing knowledge in this area could lead to more precise concepts of practical value to the clinician.

Such efforts as these can only lead to scientific progress, the aim of the Academy in sponsoring its conferences. No doubt subsequent discussions will be designed to study further problems in the areas outlined in the first conference.

The primary concern of the International Academy of Oral Pathology with scientific problems rather than with the socioeconomic aspects of the specialty was evident in the agenda for this first conference. The trustees are of the opinion that this is as it should be since they feel that, by increasing and extending the scope of scientific interest among oral pathologists, it is likely that this specialty will find wider acceptance by practicing dentists.

Of equal importance is the recognition of a wide range of oral diseases as being within the primary interest of the oral pathologist. Thus, those with such training—physicians or dentists—are considered to be more than morbid anatomists, having a clear interest in the clinical aspects of oral disease.

These and other concepts are the natural outgrowth of experience in many countries in the postwar period. This has been particularly evident in the United States, where oral pathology as a specialty has been drawn into discussions on the reorientation of the special areas of dentistry.

The success of this first activity of the Academy is indeed noteworthy, and we extend to it our congratulations. Soon the proceedings of the conference will be published and made available to all who have an interest in oral pathology.

K. H. T.

ANNOUNCEMENTS

American Institute of Oral Biology Case History Service

The Institute continues to offer case histories from the broad field of oral biology for the year 1959-60. These will include original 35 mm. Kodachrome slides of pathologic conditions of the oral cavity and jaws, accompanied by pertinent laboratory findings, medical background, roentgenograms, photomicrographs, diagnostic criteria, and whatever else may be indicated in each individual case, with a "general discussion" of the disease. A loose-leaf binder and matching Kodachrome slide box will be furnished. The fiscal year of the Institute runs from October 1 to September 30.

This monthly service was initiated in 1952 and has met with outstanding success. During these seven years it has provided a total of 1,011 one-year subscriptions and the histories were accompanied by 148 Kodachrome slides.

The subscriber to this case history service is entitled to full membership in the American Institute of Dental Medicine. Members of the A. D. A. or A. M. A., or their foreign equivalent, are eligible to apply. Due to the great demand for this service, it is recommended that those interested subscribe at an early date for immediate delivery. An index of the various diseases covered during this period will be mailed upon request. Complete series for the years 1954 to 1958 are still available; unfortunately, the series for 1952 and 1953 are out of print.

For further information, address all communications to the secretary, Mrs. C. Novembri, 2240 Channing Way, Berkeley 4, California.

Armed Forces Institute of Pathology

The Dental and Oral Pathology Division announces its annual course entitled "Pathology of the Oral Regions." This course will be presented during the period March 14 to 18, 1960.

The material presented will be directed at the biologic aspects of general dental practice. Attendance is limited to 100, and requests should be made immediately since registration is very heavy.

First District Dental Society

The Section on Oral Surgery will meet at 8 P.M. on Wednesday, Nov. 18, 1959, at the First District Dental Society, on the eighteenth floor of Hotel Statler, New York, New York. Dr. Harry Blechman will read a paper on "Microbiological Considerations in Oral Surgery."

Veterans Administration Medical Teaching Group Hospital

The Veterans Administration Medical Teaching Group Hospital of Memphis, Tennessee, announces that one rotating dental internship and one residency in prosthodontia will be available for the year beginning July 1, 1960.

Information and application forms may be obtained from the Chief, Dental Service, Veterans Administration Medical Teaching Group Hospital, Memphis, Tennessee.

University of Minnesota School of Dentistry

The third annual course in Advanced Oral Pathology for 1960 will be held from Thursday, April 21, through Tuesday, April 26, 1960. About one-half of the time is devoted to examination of approximately 200 slides. The subjects and lecturers will include the following:

1. Salivary Gland Pathology. Dr. John T. Godwin, Professor of Pathology, Emory University, Atlanta, Georgia.
2. Bone Pathology. Dr. Louis Lichtenstein, Chief of Pathology, Veterans Administration, Los Angeles, California.
3. Advanced Roentgenographic Diagnosis of Diseases of the Jaws. Dr. Edward Stafne, Professor Emeritus, Mayo Clinic, Rochester, Minnesota.
4. Pathology of Soft Tissues. Dr. Richard Shuman, Chief, Department of Pathology, Norfolk General Hospital, Norfolk, Virginia.
5. Roentgenographic Technics for the Head and Neck. Dr. Richard W. Moss, Chief, Oral Surgery Section, Veterans Administration Center, Wood, Wisconsin.
6. Dermatopathology. Dr. Robert Goltz, Professor of Dermatology, School of Medicine, University of Minnesota, Minneapolis, Minnesota.
7. Odontogenic Tumors. Dr. Robert J. Gorlin, Professor of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis, Minnesota.
8. Oral Manifestations of Systemic Disease. Dr. Anand Chaudhry, Professor of Oral Pathology, School of Dentistry, University of Minnesota, Minneapolis, Minnesota.

The course will be limited to twenty participants. Tuition will be $100.00. Interested persons will please contact Dr. Robert J. Gorlin, Professor and Chairman Division of Oral Pathology School of Dentistry, University of Minnesota, Minneapolis 14, Minnesota.

Canadian Dental Association

The National Convention of the Canadian Dental Association will be held Sept. 25 to 28, 1960, in Ottawa, Ontario, Canada.

Mount Sinai Hospital

The Division of Oral Pathology will present monthly clinical oral pathology conferences on the second Friday of each month except December from November through May.

The first conference will be held at 5 P.M. on Nov. 13, 1959, in Lecture Room 3B on the third floor of the main building of the Mount Sinai Hospital in New York City. Dr. Lester Cahn will speak on "White Lesions of the Mouth."

Western Society of Periodontology

The Western Society of Periodontology will hold its seventh annual Las Vegas meeting March 27, 28, and 29, 1960. The speaker will be Dr. Hans Selye.

For further information, please direct inquiries to Dr. Howard A. Tyrrell, 1508 North Sycamore St., Santa Ana, California.

New York University

Two new $3,400.00 fellowships in dental care for the chronically ill and handicapped are being offered for the 1959-1960 academic year by the New York University College of

Dentistry. The fellowships are supported in part by a grant from the Office of Vocational Rehabilitation of the United States Department of Health, Education, and Welfare.

Further information on the fellowships can be obtained by writing to Dr. Sidney I. Silverman, Director, Graduate and Postgraduate Division of Prosthodontics, College of Dentistry, New York University, 421 First Ave., New York 10, New York.

University of Pennsylvania

The following postgraduate courses are announced by the School of Dentistry:

Hypnosis Applied to Dentistry. Nov. 30 to Dec. 2, 1959. William T. Heron.

The Use of Ultrasonics in Periodontia. Dec. 12, 1959. Henry M. Goldman and D. Walter Cohen.

Oral Diagnosis and Roentgenology. Jan. 4 to 8, 1960. Lester W. Burket and LeRoy M. Ennis.

Prosthetic Relations of the Temporomandibular Joint. Jan. 18 to 22, 1960. Ernest R. Granger.

Hospital Dentistry. Jan. 25 to 27, 1960. John P. Looby and associates.

Practice Administration. March 7 and 8, 1960. Harry M. Klenda.

University of Pennsylvania Announces Clinical Fellowships in Oral Pathology

A clinical fellowship in oral pathology, supported by the American Cancer Society, at the University of Pennsylvania School of Dentistry is open to qualified applicants. A tax-free stipend of $3,600.00 accompanies the fellowship for one year beginning July 1, 1960. Applications should include a curriculum vitae, academic record in dental school, and at least two letters of reference. The deadline for receipt of all credentials is March 15, 1960.

All applications and inquiries should be addressed to the Committee on Fellowships and Traineeships, 4001 Spruce St., Philadelphia 4, Pennsylvania.

University of Texas M. D. Anderson Hospital and Tumor Institute

The University of Texas M. D. Anderson Hospital and Tumor Institute announces the fourteenth annual symposium on fundamental cancer research, "Cell Physiology of Neoplasia," to be held Feb. 25, 26, and 27, 1960. Dr. T. C. Hsu, head of the Section of Experimental Cytology, Department of Biology, M. D. Anderson Hospital, is chairman of the Symposium Committee.

Further information may be obtained by writing the Editorial Office, University of Texas M. D. Anderson Hospital, Texas Medical Center, Houston 25, Texas.

Tufts University

Tufts University School of Dental Medicine announces the following postgraduate refresher courses:

DPG. 201. Oral Pathology for the Oral Surgeon. Nine Thursday afternoons, Feb. 4 through March 31, 1960. Irving Glickman, Gerald Shklar, and Irving Meyer. Tuition, $150.00.

DPG. 708 Oral Rehabilitation. Feb. 25 to 27, 1960. Jerome M. Schweitzer. Tuition, $100.00.

DPG. 707. Crown and Bridge Prosthesis (Participation Course). Jan 18 to 22, 1960. R. Sheldon Stein. Tuition, $200.00.

DPG. 709 Special Postgraduate Refresher Course in Prothetics for the Periodontal Patient. May 9 to 12, 1960. Irving Glickman and staff. Tuition, $150.00.

DPG. 602. Clinical Adjustment of the Occlusion. March 14 to 16, 1960. Bernard Jankelson. Tuition, $100.00.

DPG. 402. Cephalographics and Diagnosis. Jan 20 to 22, 1960. Herbert I. Margolis and staff. Tuition, $100.00. (Applicants must be members of the American Association of Orthodontists or an equivalent foreign society.)

DPG. 401. Orthodontic Principles of Interest to the General Practitioner. Eight Wednesdays, Feb. 10 to March 30, 1960. Herbert I. Margolis and staff. Tuition, $150.00.

DPG. 501. Clinical Dentistry for Children. Jan. 28 and 29, 1960. Bernard Rabinowitch, Beverly Hills, Calif. Tuition, $50.00.

Further information and application forms may be obtained by writing Division of Graduate and Postgraduate Studies, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.

Tufts University Announces Research Fellowships

Tufts University School of Dental Medicine announces two research fellowships in oral pathology and periodontology for the school year beginning in September, 1960. The fellowships are intended for graduate dentists interested in research and teaching careers in oral pathology and periodontology. There is an annual stipend of $5,000.00, and the fellowships are renewable.

Additional information and application may be obtained from Dr. Irving Glickman, Department of Oral Pathology and Periodontology, Tufts University School of Dental Medicine, 136 Harrison Ave., Boston 11, Massachusetts.